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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 33 MAY, 1953 NO. 5

Original Communications

NEW INSTRUMENTS FOR CARDIAC SURGERY

A. M. DOGLIOTTI, M.D.,* AND G. GUGLIELMINI, M.D.,** TURIN, ITALY

WE WISH to present some technical alterations we have introduced in the execution of therapeutic interventions for Fallot's tetralogy and for mitral stenosis.

SURGERY OF FALLOT'S TETRALOGY

Our surgical experience has made clear that the instruments used by different authors, both in Blalock's and in Potts' operations, are not always easily handled and far from being free of criticism.

Many criticisms could be made, for instance, about the use of the vascular clamp proposed by Potts for aortic pulmonary anastomosis:

1. It is difficult to be placed, because of the need for an all-round isolation of the aorta and the consequent necessity of a double ligature of the many collateral branches, which are often hypertrophied owing to the conspicuous compensating circulation.
2. It is difficult to anchor the pulmonary artery to the clamp in order to perform the vascular suture.
3. It is difficult to withdraw the posterior branch of the clamp when the anastomosis is performed.

On its turn, Blalock's clamp requires a full all-round isolation of the pulmonary artery, thus completely cutting off the blood stream in it; besides, it does not allow a complete immobilization of the vessel or the fixation of the terminal end of the subclavian artery to the pulmonary itself.

In order to facilitate the technique of blood vessel anastomosis, both of the laterolateral type and the terminolateral type, several clamps were devised by different authors, mostly two-branched clamps, all devised in order to keep the blood stream uninterrupted (Southwick, Julian and Fildes, Large, Johnston and Preshaw, Freeman, and others).

According to our opinion, all these instruments have not the necessary requirements for the practice of vessel anastomosis in general, especially for aortic pulmonary anastomosis and subclavian-pulmonary anastomosis.

Received for publication, Dec. 2, 1952.

*Professor of Surgery and Director of the Surgical Clinic of The University of Turin.
**Assistant Professor of Surgery, University of Turin.

We think that the three-branch clamp, which we are presenting, possesses all the necessary requirements. This clamp is composed of two main parts: the shaft and the three branches for vessel compression. The shaft, with a square section, is composed of three gliding rods, one inside the other, each one connected with one of the three branches.

These have a half-hexagon shape; the proximal and distal branches must be stronger than the middle one. All surfaces coming in contact with blood vessels are finely indented to avoid slipping. The ends of the branches, as well as all external surfaces, must be rounded and smooth to avoid any lesion to the surrounding vascular and connective formations.

The movements of clinching and releasing the proximal and distal branches onto the medial branch are independent one from the other; both are activated by screws which are governed by two nuts placed on the upper end of the shaft.

The practical application of our clamp has shown that it is possible to operate, easily and safely, any laterolateral or terminoterminal anastomosis, both in the field of cardiac and of other vessel surgery (portal hypertension, vessel grafts, etc.).

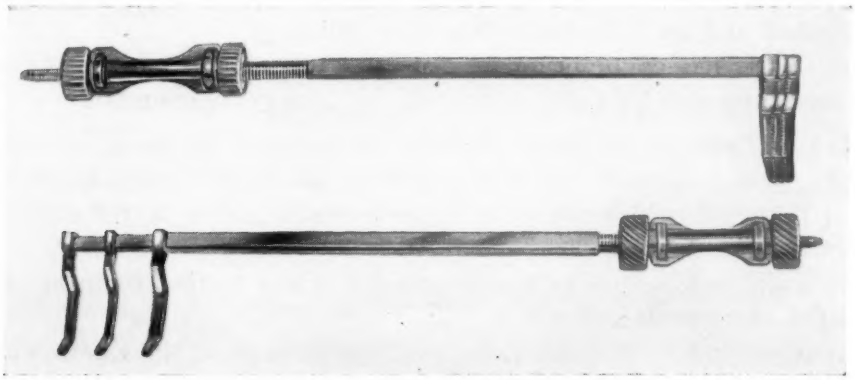


Fig. 1.—Three-branched clamp.

A. *Potts' Operation.*—

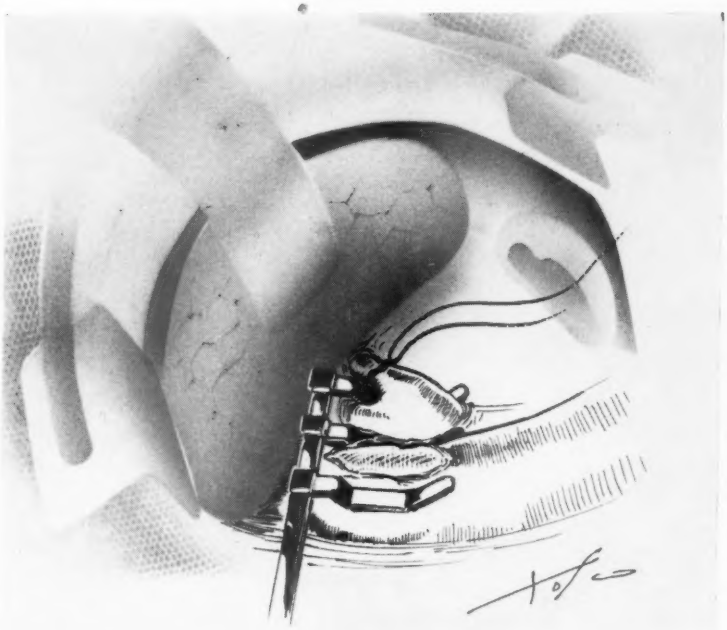
Surgical exposure of the area of great vessels: A left lateral thoracotomy is performed.

Isolation of the upper surface of the pulmonary artery and its upper lobar branch: A Carrel clamp or a temporary ligature must be applied to the upper branch to avoid pulmonary reflux circulation. It is enough to set free from the adventitious membranes a length of about 3 or 4 cm. on the upper surface of the artery. When the pulmonary artery is very large it is not necessary to set free its lobar upper branch, since it is enough to do that for a certain length of the upper surface of its main trunk and afterward to seize a fold of it between the distal branches of our clamp.

Isolation and denudation of the anteromedial surface of the aorta: Isolation and denudation are performed to the extent of a few centimeters.

Setting of the clamp: The distal branch is introduced between the two lobar branches of the pulmonary artery, the medial branch resting between the two vessels to be anastomosed, with the proximal one ready to receive the desired portion of the aorta (Fig. 2). First the closure of the branches on the pulmonary artery is made; then, having stretched by means of an Allis

Fig. 2.



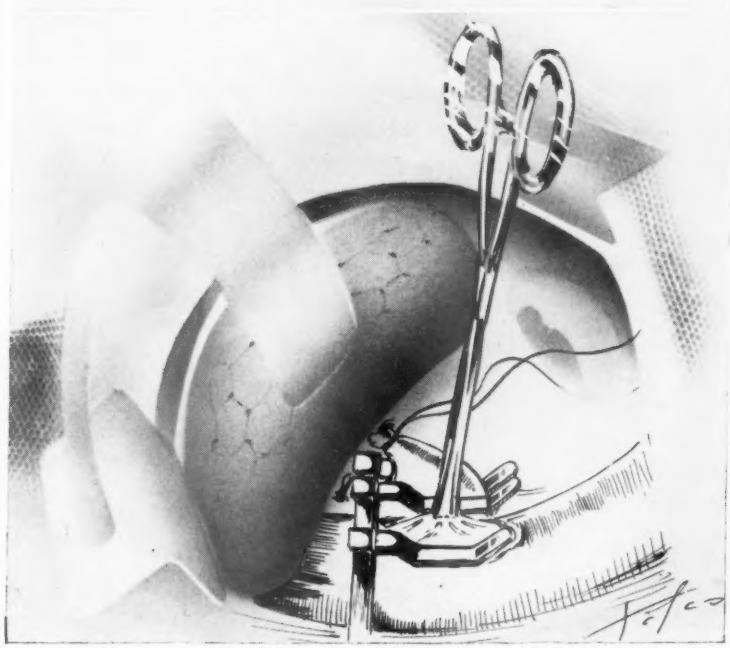


Fig. 3.

clamp with very tiny teeth a large fold on the wall of the aorta, the fold is clenched between the proximal and the medial branches (Fig. 3).

The two partial segments of the vessels are then raised up to the same level and put in contact with a single clamp, thus being joined one to the other and reciprocally locked together. The blood stream flows uninterrupted both in the aorta and in the pulmonary artery.

Fig. 4.

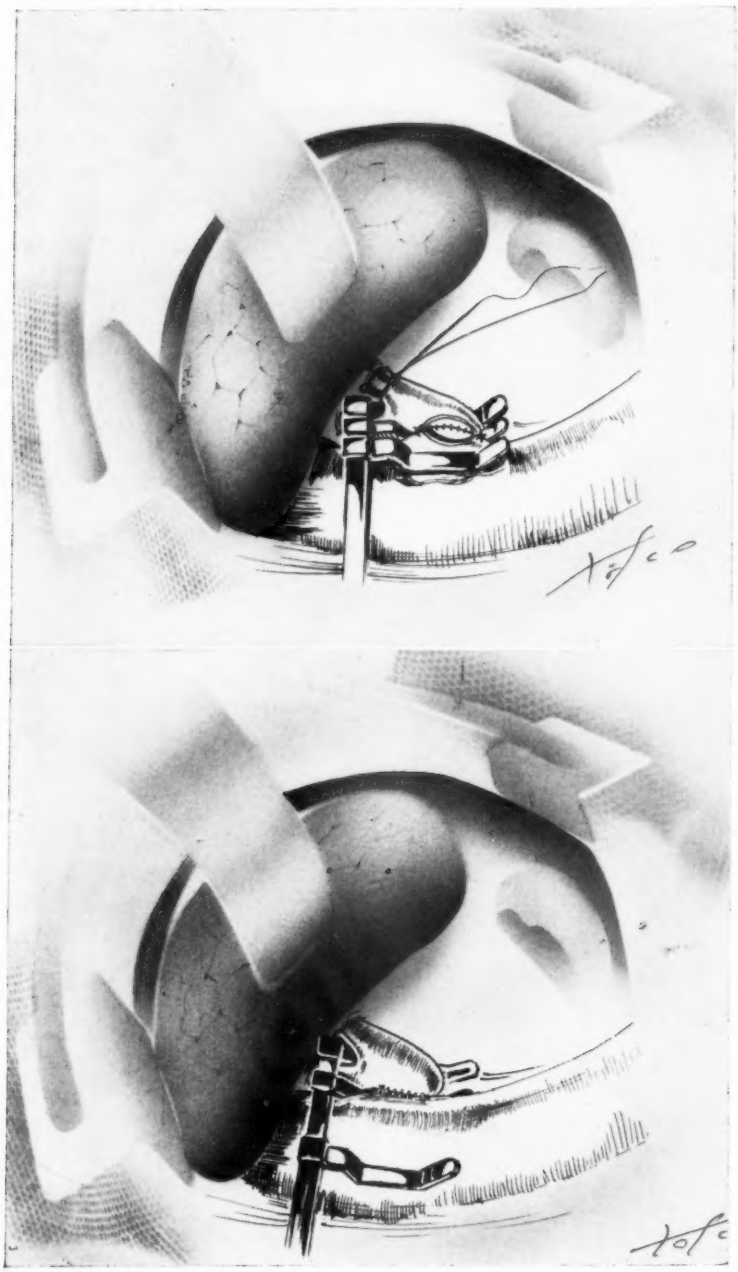


Fig. 5.

The whole technique of anastomosis is noticeably easier and brought to an end in a shorter time (Fig. 4).

The removal of the clamp: This procedure is very easy. The compressing branches are released, first the branch on the pulmonary artery, then the branch on the aorta. The instrument is then removed with a rotary clockwise movement (Fig. 5).

B. *Blalock's Operation.—*

Thoracotomy of the third or fourth intercostal space: Anterior thoracotomy on the third intercostal space, or lateral thoracotomy on the fourth space is performed.

Isolation of the pulmonary artery: The pulmonary artery, anterosuperior surface, is isolated.

Isolation and section of the subclavian artery: Isolation and section are performed following the Blalock technique. A Carrel hemostatic clamp is applied to the origin of the artery.

Setting of the clamp: The choice of the clamp (the right-handled or left-handled one) depends upon the side of the operation.

The setting of the selected clamp is not difficult. A fold of the pulmonary artery, duly seized and stretched out with a fine-toothed Allis clamp is held between two branches.

The terminal end of the subclavian artery, freed from its perivascular lining, is introduced between the two other branches (Fig. 6). The two vessels are thus near each other and kept still and in contact by means of our instrument (Figs. 7 and 8).

Opening of the branches: When the anastomosis is performed, the opening of the branches follows in the same order: the pulmonary artery first, then the subclavian. The instrument is easily removed with a rotary movement, so that the branches will glide below the anastomosis.

CONCLUSIONS

While performing the aortic pulmonary anastomosis, our three-branched clamp (angiostat) has the following advantages:

1. It does not require an all-round isolation of the aorta, thus avoiding greater risks and waste of time.

2. It allows several arterial vessels, very important for the collateral circulation, to be maintained.

In both Blalock's and Potts' operations:

1. It does not require the full isolation of a long tract of the pulmonary artery and allows the circulation in this vessel during the whole operation.

2. The setting and the removal are both easy, quick, and free of all dangers.

3. It allows the anastomosis to be performed in a much shorter time.

4. It keeps together, firmly joined and meeting each other, the edges of the two vessels to be anastomosed; the suture is then more easily made.

5. Its application is possible in all cases of Fallot's tetralogy, whether the operation be performed through a right or a left thoracotomy.

Fig. 6.

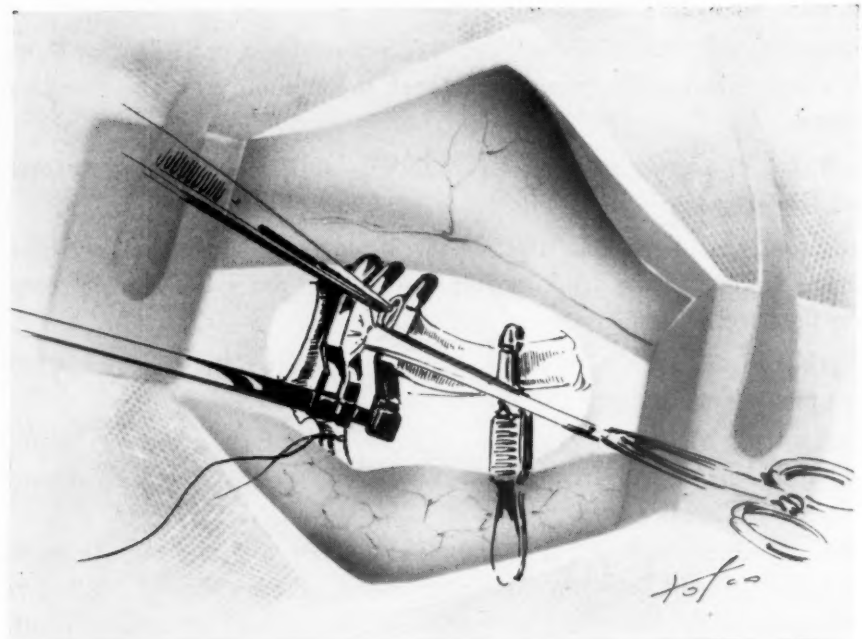
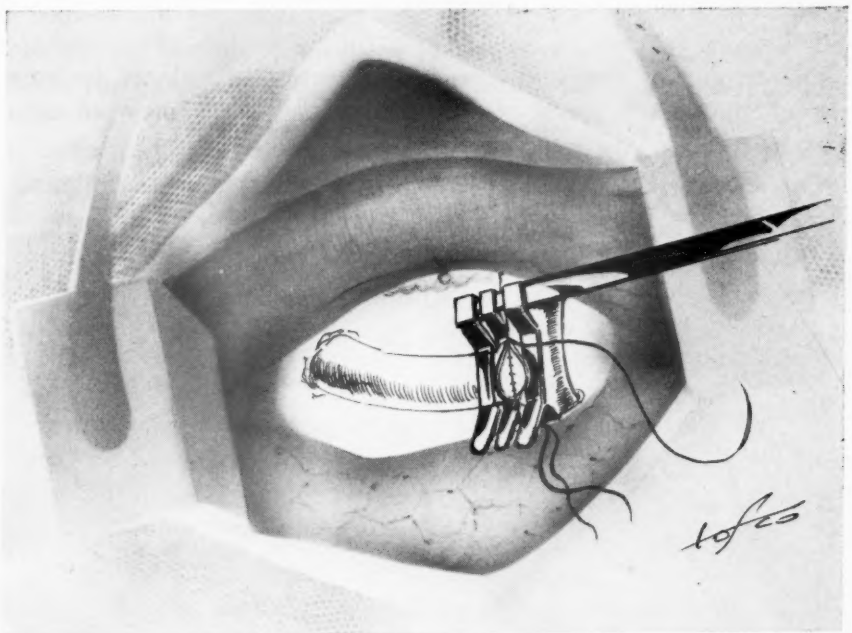


Fig. 7.

Finally, we think we can safely claim, through personal experience based on more than thirty cases, that our clamp can be usefully and adequately employed in the more general field of all vascular anastomoses, mainly when the blood circulation in the vessels must be maintained during such operations as those involving the anastomoses of portacaval, splenorenal, and carotid-jugular veins.

Fig. 8.



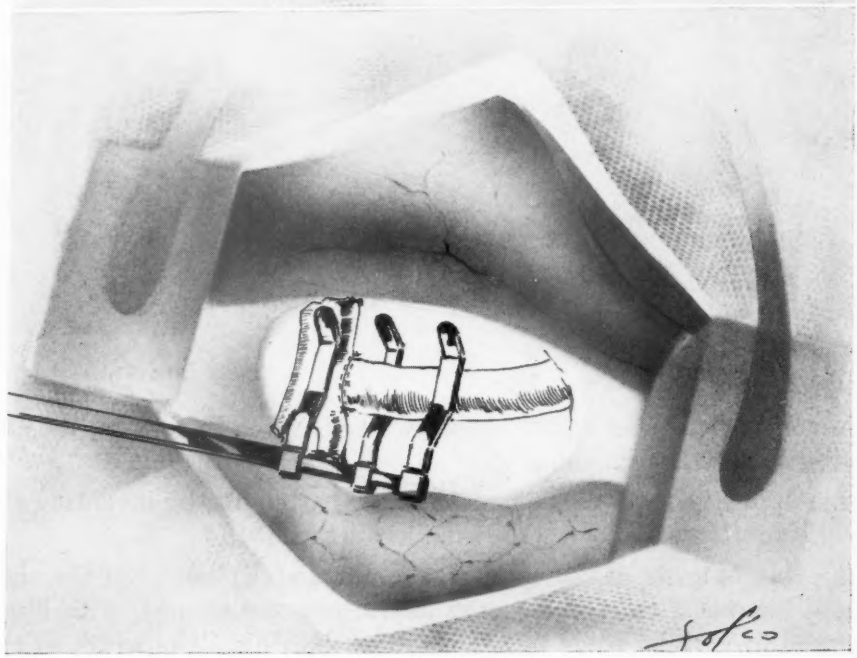


Fig. 9.

SURGICAL TREATMENT OF MITRAL STENOSIS

The variety of the proposed instruments for mitral commissurotomy suggests that none of them is absolutely successful. The use of the various instruments proposed by several authors allows us to point out the following disadvantages:

1. A good deal of refluxed blood collects in the newly formed space between the finger, which was introduced in the atrium, and the shaft of the instrument.

2. The exploring finger increases noticeably in volume because of the presence of the instrument's shaft. The vessel walls may be occasionally damaged, when the space is too narrow.

3. The endoatrial work of a shafted instrument is quite difficult.

Fig. 10.

Fig. 11.

In our opinion the greatest disadvantage is given by making the exploring finger itself a cutting instrument.

This difficulty we overcame, after several attempts, by inventing the "valvulotomic ring" which we are showing here (Fig. 10).

The ring is made of the exact size of the distal phalanx of the right forefinger; it carries a tiny blade, very sharp, crescent-shaped, with blunt ends, and placed at a right angle to the plane of the ring. The width of the blade at the central point ranges from 3 to 5 mm.

The use of our valvulotomic ring in the commissurotomy may be described as follows:

The atrial cavity having been explored according to the rules of cardiosurgical technique, a first dilatation is performed with the finger.

When this is not sufficient and it is advisable to adopt an instrumental dilatation, the finger is withdrawn and the auricle is temporarily shut with a clamp.

The rubber glove is taken off, and the valvulotomic ring is placed on the right forefinger. The blade is placed on the very spot where, during the first exploration, the anterolateral (or the posteromedial, if necessary) commissure was located.

A new rubber glove is put on again and a small incision is made so that only the cutting edge of the blade juts out.

The finger is introduced again in the mitral atrium, according to the direction remarked during the first exploration. The commissure practically cuts itself on the blade supported by the finger (Fig. 11). If necessary this action can be repeated.

After the finger is withdrawn, the previously prepared pouch at the basis of the auricle must be closed; the suture is reinforced with a few silk stitches and the operation is quickly completed.

The use of the valvulotomic ring in twenty cases has proved its safety, efficiency, and quick employment.

AUTOLOGOUS TISSUE TUBES FOR AORTIC GRAFTS IN DOGS

E. Converse Peirce, II, M.D., Baltimore, Md.

(From the Cardiovascular Clinic, United States Public Health Service Hospital—Baltimore, Clinic of Experimental Medicine and Therapeutics of the National Heart Institute, Federal Security Agency)

AORTIC grafts using viable and nonviable homologous tissue have been initially successful in dogs and human beings.[3-6, 9-12, 16, 20] The most promising variety of graft from the standpoint of freedom from failure in animals has been that which employs viably preserved homologous tissue, since for a time it acts as an autologous graft.[15] All homologous grafts, however, undergo progressive degeneration and after a period of perhaps three to six months are very similar, the original tissue persisting as a devitalized support for a new heavy intima and adventitia supplied by the host. Except for microscopic changes and gross loss of elasticity many of these grafts resemble normal aorta. Others, however, show intimal ulcers, calcification, bone formation, mural thrombi, and other changes not seen in autologous arterial or venous grafts.[15] None of the homologous grafts have been followed long enough to determine their end results, although changes are expected to take place only slowly after the first six months. It would thus appear that autologous grafts which do not degenerate are at least theoretically superior to homologous grafts which do. Grafts of autologous vein to artery have been used occasionally since their study in the early part of this century[1] and should probably be used by choice when a suitable vein is readily available.[8] Autologous veins, however, are not available for aortic replacement and the procurement of even smaller ones may dangerously prolong a complicated operative procedure.[19]

We have investigated the possibility of producing artificial autologous arteries since 1948, following the observation that polyethylene implanted in a dog may result in the production of a smooth, tough, fibroserous membrane. Following preliminary studies to determine the best site and method of implantation of the plastic, the character of the membrane lining cells, and the optimal implantation time, a fairly satisfactory method of producing tissue tubes large enough for aortic implantation has been developed. The grafts are thinner than desired but have, nevertheless, proved successful and have carried blood without important dilatation or degeneration for periods up to thirty months.

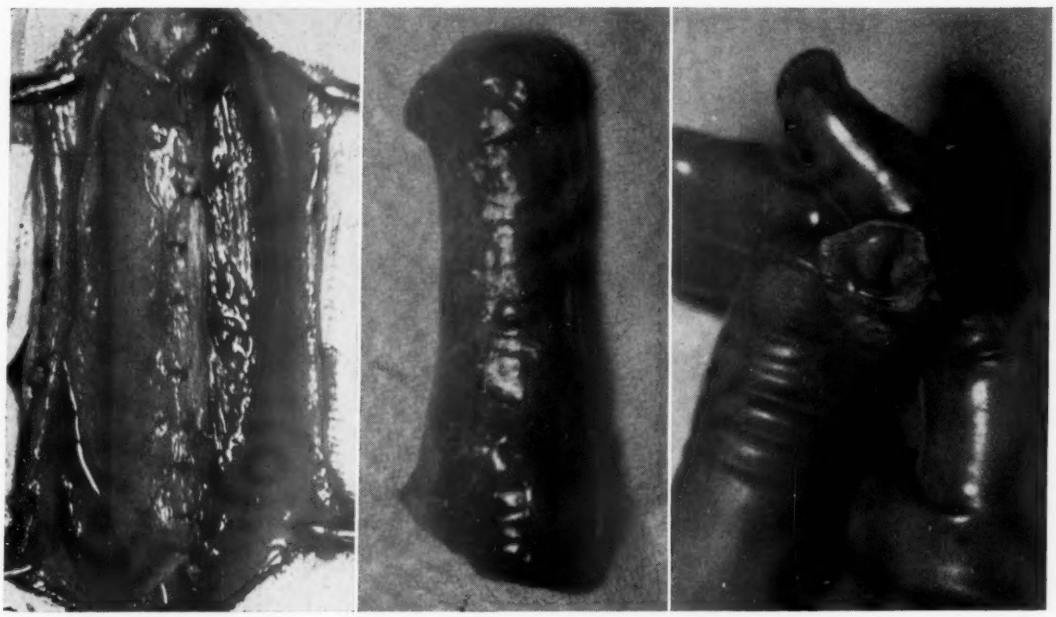
MATERIALS AND METHODS

Mongrel dogs of 8 to 24 kilograms were subjected to a two-stage procedure. Intravenous pentobarbital sodium (Nembutal) was used for anesthesia. The anterior rectus sheath on one or both sides was exposed through an 8 to 10 cm. paramedian incision. The outer and inner borders of the sheath were divided and partially separated from the underlying muscle. A sealed polyethylene

Received for publication, June 27, 1952.

tube 5 to 8 cm. in length and 0.6 to 1.0 cm. in diameter was placed in this fascial trough which was then closed over it and at both ends with interrupted 0000 waxed silk (Fig. 1, *A*). The subcutaneous and subcuticular layers were similarly closed. Penicillin was given postoperatively to some of the animals and, in a few, effusions or hematomas about the tubes were aspirated.

Five weeks or longer after implantation, the second stage was carried out. The dogs were again anesthetized with pentobarbital sodium in the postabsorptive state. A long rectus incision was made on the side of the tube insertion. The tube and surrounding fascia were removed en bloc with as little excess tissue as possible (Fig. 1, *B*). The ends of the tube were cut off and saved for histologic study together with a second tube, if it had been implanted.



A. *B.* *C.*

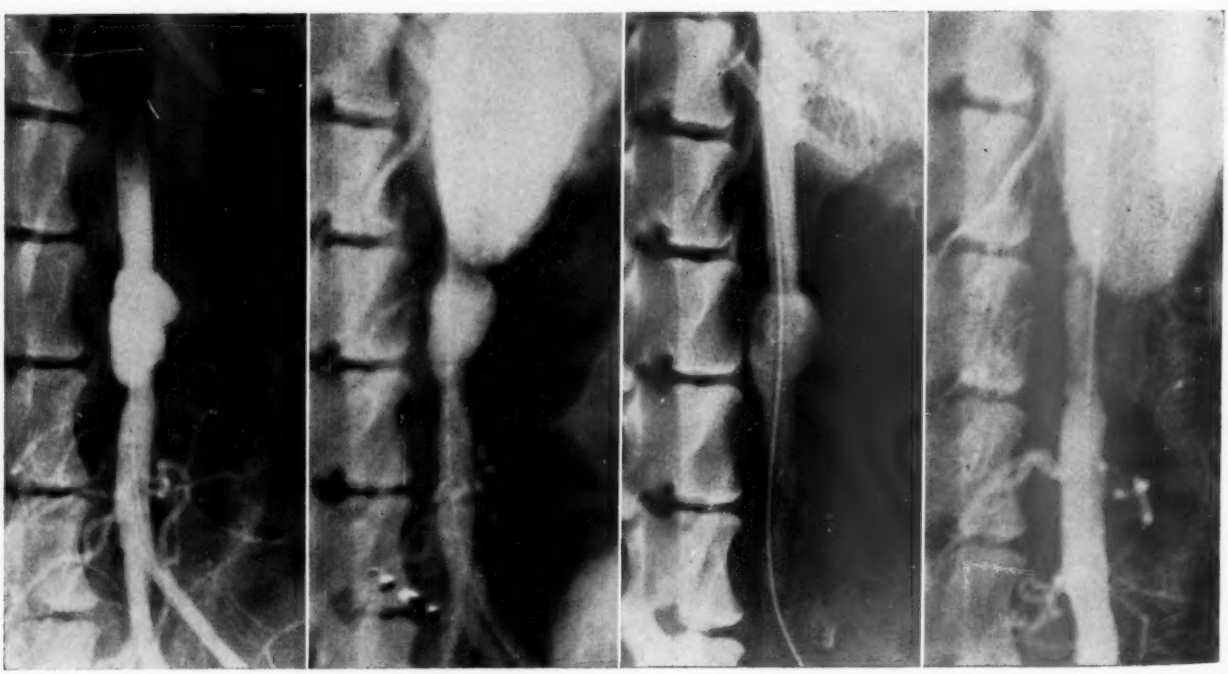
Fig. 1.—*A* (No. 17-49), A polyethylene tube implanted in the anterior rectus sheath with 0000 silk sutures. The ends have been partially sutured to prevent extrusion of the polyethylene.

B (No. 74-49), Tissue tube freshly removed from the abdominal wall eight weeks after polyethylene implantation.

C, The tube shown in *B* opened preparatory to its use as a graft. It grossly resembles an artery and has a smooth glistening lining.

If the tissue tube was satisfactory grossly, with a reasonably thick wall and a smooth glistening lining (Fig. 1, *C*), it was implanted in the abdominal aorta between the renal arteries and inferior mesenteric artery by using a continuous everting mattress suture of 00000 arterial silk as previously described.[16] Generally, a portion of aorta was excised and discarded. Suture was greatly facilitated by leaving the cut polyethylene tube in place until two proximal and two distal stay sutures had been placed. There was a tendency for the fascial and new fibrous layers to separate; this had to be prevented by making sure that sutures included both layers. On release of clamps only occasional additional sutures were required (Fig. 2). The posterior peritoneum was approximated

Fig. 2 (No. 122-49).—Tissue tube freshly grafted into the abdominal aorta. The caliber approximates that of the host aorta. Dog died of shock postoperatively.



A. *B.* *C.* *D.*

Fig. 3.—*A* (No. 97-49), Graft at five days.

B, Graft in *A* at four months.

C, Graft in *A* at sixteen months. The tube which was moderately dilated and quite irregular when grafted has become smoother and has not shown progressive enlargement. There was no essential change at thirty months.

D (No. 114-49), Tissue tube at twelve months. There is slight irregularity in the vicinity of the suture lines but there is no tendency toward dilatation.

over the anastamosis and the anterior abdominal wall was closed in layers. Except for occasional doses of penicillin, no special postoperative treatment was given.

Animals were followed by palpatation of femoral pulses at weekly intervals and by catheter aortography,[13] generally within two to four weeks of the second stage and then every six to twelve months until sacrifice (Fig. 3). Portions of the fresh tissue tubes and entire grafts at sacrifice were studied by surface staining of their lining with silver nitrate[14] as well as by the usual histologic methods.

RESULTS

The results in ten tissue tube grafts are given in Table I. A good many additional first-stage procedures were carried out for preliminary study while, in other instances, the tubes were unsatisfactory and consequently discarded. In two instances the dogs died of shock following the second operation and have been excluded, since this is unusual and without direct bearing on the value of the tubes. A total of about forty dogs were used in this study.

In the early part of the work, open-ended polyethylene tubes were implanted. The dead space resulted in frequent aseptic effusions, the tubes tended to be unpredictably larger than the prostheses, and their linings were frequently irregular. By closing the tubes the dead space was eliminated and tubes of predictable caliber with good linings were produced. Other sources of tube loss were reaction about the silk sutures and extrusion of the polyethylene from the fascial cuff. It is felt that the use of finer or less reactive sutures and the careful closure of the fascia over the ends of the polyethylene will generally eliminate these difficulties.

Most of the tubes fitted the polyethylene snugly and had a smooth lining. They grossly resembled thin-walled blood vessels (Fig. 1, *C*) and did not seem reliably to increase in thickness if the first stage was prolonged beyond six weeks. The tubes were thinner and did not handle as well as arteries. During suturing they had a tendency to split into two layers, a new inner fibroserous and an old outer fascial layer. The inner layer was frequently lined by flattened cells resembling endothelium on surface silver staining (Fig. 4, *A*). It varied considerably in cellularity and thickness but generally showed well-oriented collagenous bundles but no elastic tissue (Fig. 5). The fascial layer showed a normal component of heavy collagen bundles with fine interspersed elastic fibers (Fig. 4, *B*).

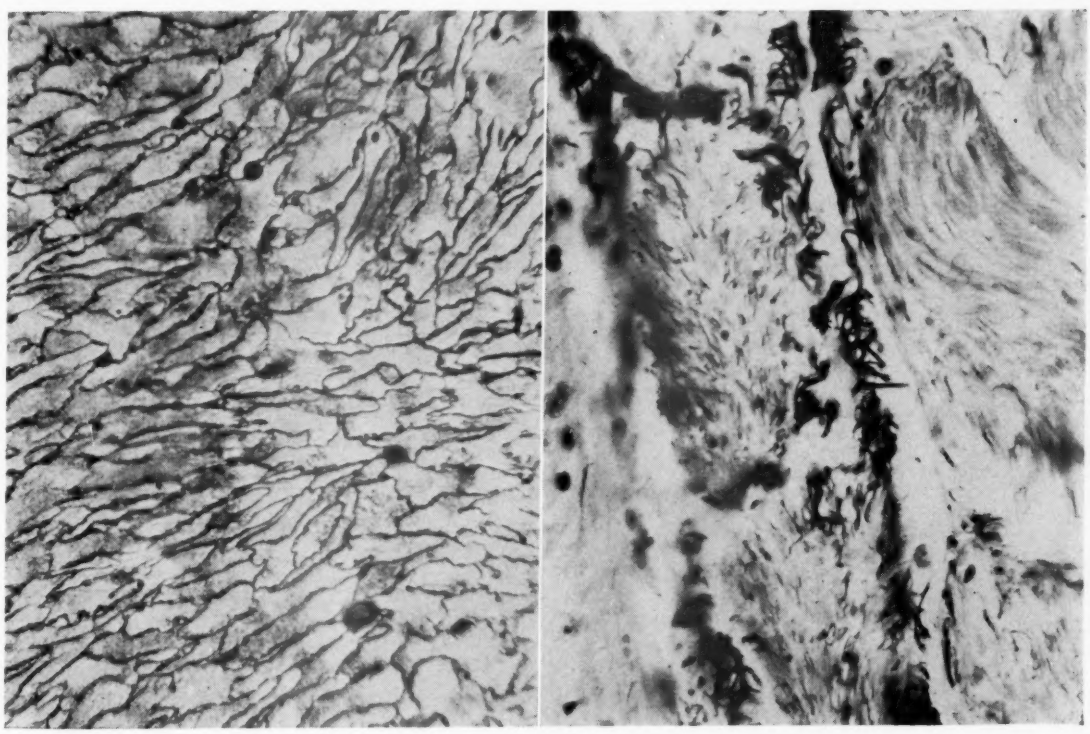
Of the ten implanted tubes, one failed completely as the result of infection. The animal died from hemorrhage on the eleventh day. The nine remaining tubes carried blood satisfactorily. One dog died at ten weeks from pneumonia and a large mural thrombus was present at one suture line, considerably narrowing the lumen. The remaining eight grafts, varying from 2.5 to 4.5 cm. in length, have been entirely satisfactory from a functional standpoint. Five of these grafts were too large at implantation and have remained so, with little or no tendency to dilate progressively, as shown by periodic aortograms (Fig. 3, *A*, *B*, and *C*). Dilated grafts have shown minor irregularities including mural thrombi at sacrifice (Fig. 6, *A*). Four animals are still alive at

TABLE I. RESULTS IN TEN COMPLETED TISSUE TUBE GRAFTS

NUMBER	WEIGHT (KG.)	DURATION	AORTOGRAMS	CAUSE OF DEATH	GROSS RESULT	MICROSCOPIC RESULT
103-49	23	11 days	None	Infection with dissection	Dehiscence.	Very marked inflammation. Numerous bacteria.
74-49	20	70 days	7 days: Mural thrombus (large), inferior suture line.	Pneuomina	Mural thrombus over inferior portion graft.	Thrombus organized in part. Heavy fibrous wall with good preservation of fascia.
120-49	8	6 months	2 months: 2 by 4.2 cm., irregular. 6 months: 2.3 by 4.2 cm., regular.	Sacrificed	Dilated; large mural thrombus over one-third surface.	Thrombus not organized. Inner heavy fibrous wall. Good fascial layer. No degeneration. Endothelium excellent.
124-49	18	7 months	1 month: 0.8 to 1.4 by 6 cm., irregular. 6 months: 0.8 to 1.8 by 2.6 cm., irregular	Sacrificed	One dilated area with small mural thrombus.	Well oriented, heavy inner fibrous layer. Good fascial layer. No degeneration. Endothelium excellent.
114-49	16	12 months	8 days: 0.6 by 3 cm., regular 12 months: 0.8 by 2.5 cm., regular	Sacrificed	Excellent. Slight yellow discoloration.	As in No. 114-49. Small collections of hemosiderin also. Endothelium excellent.
74-50	17	14 months	6 months: 1 by 2.5 cm., slightly irregular 14 months: 1 by 2.5 cm., regular.	Sacrificed	Very good. One irregular area. Moderate yellow discoloration.	As in No. 124-49, but larger collections of hemosiderin. Endothelium excellent.
124-50	12	14 months	1 month: 1.0 by 4.3 cm., excellent. 14 months: 1.0 by 4.4 cm., excellent.	Alive		
102-49	24	26 months	6 days: 2.2 by 2.5 cm., almost round. 12 months: 2.2 by 2.6 cm. 26 months: 2.4 by 2.6 cm.	Alive		
105-49	20	27 months	12 days: 1.8 by 3 cm. 12 months: 1.8 by 3.1 cm. 27 months: 1.9 by 3.0 cm.	Alive		
97-49	22	30 months	5 days: 1.9 by 3.2 cm., irregular. 4 months: 1.9 by 3 cm., more regular. 16 months: 1.9 by 2.8 cm. 30 months: 1.8 by 2.8 cm.	Alive		

fourteen to thirty months and will be followed further (Fig. 3, *D*). Grafts of proper caliber have been entirely satisfactory (Fig. 6, *B*).

Grossly at sacrifice the tissue tubes were tougher and less elastic than the host aorta. They sometimes showed subintimal areas of yellowish discoloration but otherwise conformed to arteries in gross appearance. Microscopically there were sometimes deposits of hemosiderin, but there was no degeneration. The linings consisted of normal endothelium. The new fibrous walls were thicker and more compact than they had been at implantation. There was a decrease in cellularity and excellent circular orientation of the collagen bundles (Fig. 7). The fascia persisted in recognizable form with some decrease in cellularity but no definite change in elastic tissue. Small vessels penetrated within 0.5 mm. of the lumen, but none could be identified beyond this point.



A. *B.*

Fig. 4.—*A* (No. 15-49), Tissue tube not used for graft but silver stained for study of lining cells. In the area shown these cells very closely resemble normal endothelium. Approximately ×400.

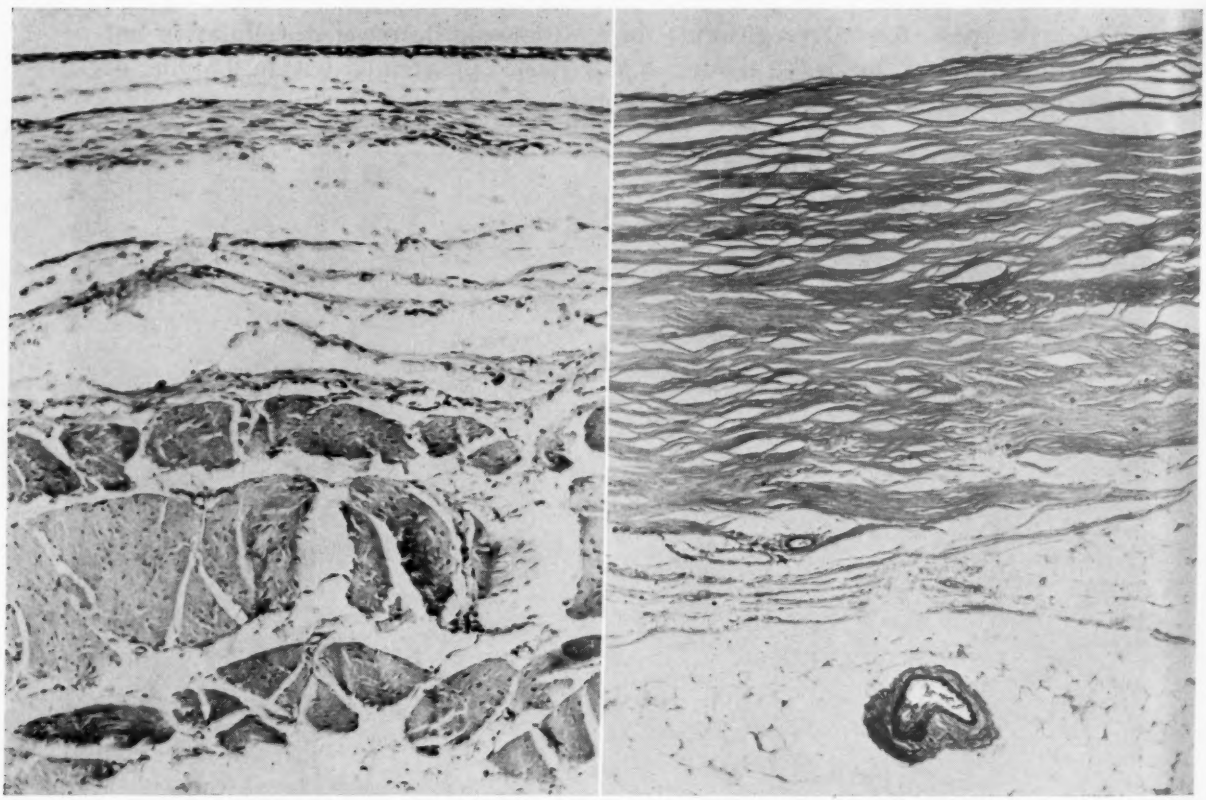
B (No. 74-49), Elastic tissue stain of fascial component of tissue tube graft. The large collagen bundles of the fascia contain fine elastic fibrils and there is a dense network of elastic tissue surrounding them. Modified van Gieson ×380.

DISCUSSION

The experimental autologous tissue tubes presented in this study consist of two components, a fibroserous lining formed by reaction about a polyethylene prosthesis and a reinforcing fascial layer formed surgically in the initial stage rather than at the time of grafting. Occasionally the inner layer is quite heavy, and this is especially true when the implantation is in the vicinity of the aorta (Fig. 5, *B*). Generally, however, the reinforcing layer is very necessary,

and, as will be shown, may explain the failure of the grafts to dilate and produce aneurysms. It is possible that fibroplastic polyethylene of a formula similar to that used for wrapping aneurysms* would produce stronger tubes, but I have been able to secure only pure polyethylene in a suitable form.

The formation of a fibroserous layer about a piece of nonreactive plastic or metal buried in tissue has been pointed out repeatedly and has been utilized to form, for example, joint surfaces.[22, 24] It would appear that fibroblasts, or possibly other cells present in loose connective tissue, readily produce a serous



A. *B.*

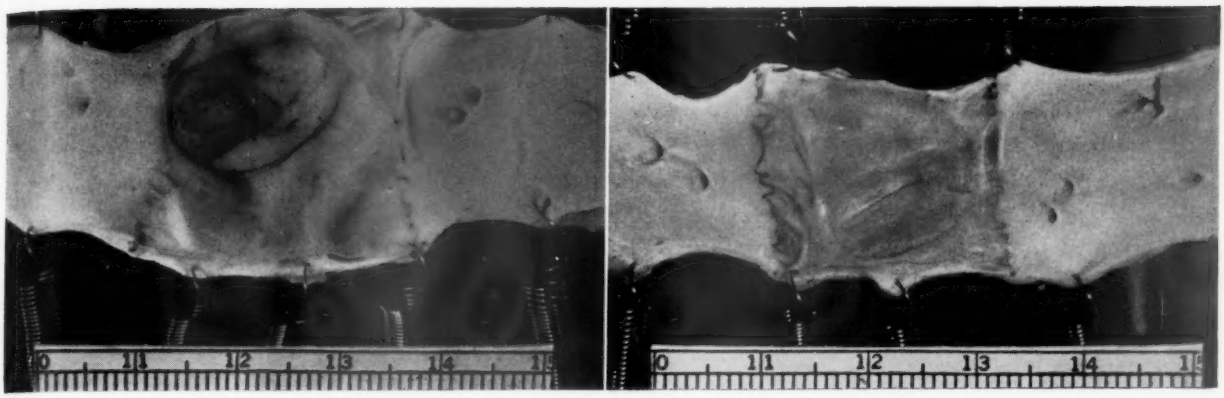
Fig. 5.—*A* (No. 13-49), Wall of tissue tube twenty-one days after polyethylene implantation. There is a thin cellular lining and a new inner fibrous layer rather loosely attached to a rather broad area of fascia containing large collagen bundles. Hematoxylin and eosin, ×160.

B (No. 30-48), Wall of tissue tube five months after polyethylene was implanted near the abdominal aorta. Such tissue tubes, regardless of time, tend to be heavier than corresponding ones made by implanting plastic in the anterior rectus sheath. Small amounts of elastic tissue are seen in the walls of a small artery and an arteriole, but not in the fibrous portion of the tube. Weigert's elastic stain, ×140.

membrane when in contact with a smooth, relatively inert surface. The fibroserous layer provides a certain amount of strength, but, more important, supplies a layer of flattened cells resembling and sometimes indistinguishable from endothelium. When used for a blood vessel graft this, of course, discourages thrombosis and extravasation of formed elements. Under certain circumstances an endothelial lining may not be necessary† but it is certainly to be desired in

*This contains dicetyl phosphate and is listed as DuPont type NV-7-14.[24]

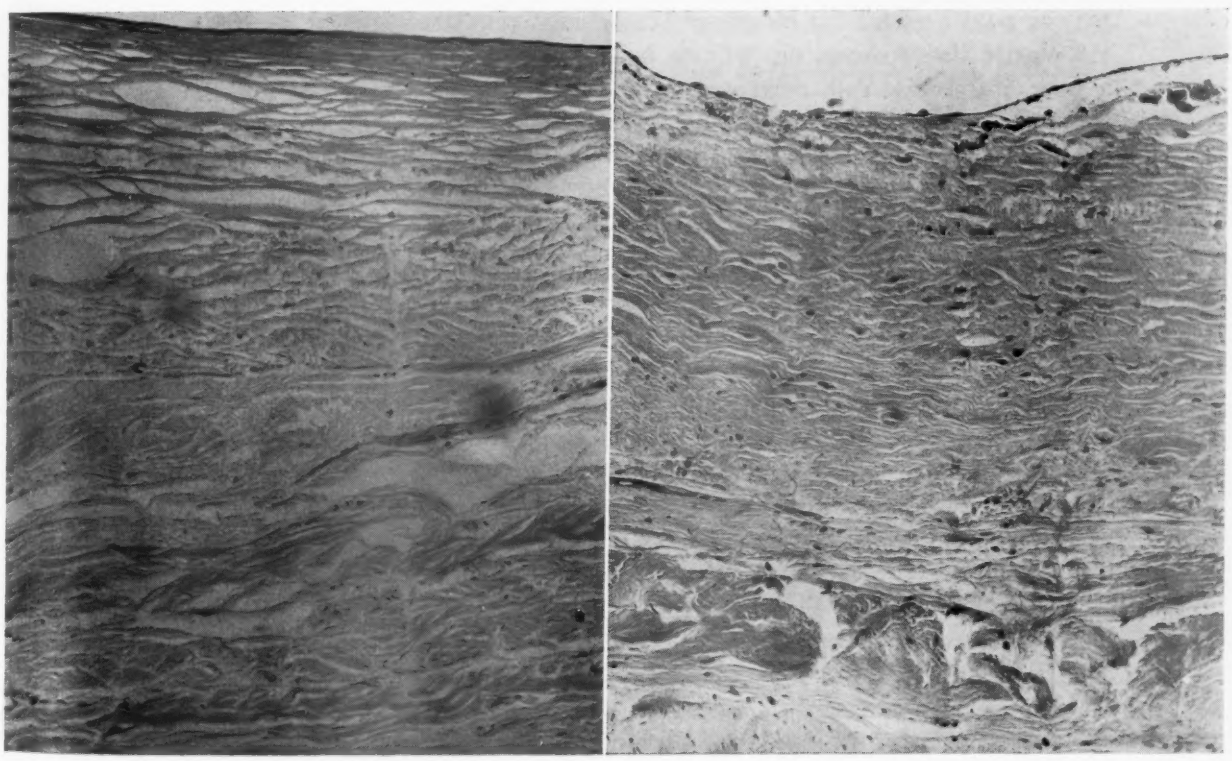
†Because (1) fascia implanted in the wall of an artery quickly becomes endothelialized,[7] (2) dissecting aneurysms occasionally form true double-barreled aortas, (3) thrombosis frequently does not occur when a segment of lining is stripped from an artery in dog or man.[23]



A. *B.*

Fig. 6.—*A* (No. 124-49), Tissue tube graft at six months. There is a dilated area containing a discrete mural thrombus. Otherwise the graft resembles a normal artery. Discoloration is the result of surface silver staining. Measurement in centimeters.

B (No. 114-49), Tissue tube graft at twelve months. There is slight irregularity of the surface which appeared largely after the graft was placed in formalin. The size and appearance are otherwise entirely satisfactory.



A. *B.*

Fig. 7.—*A* (No. 114-49), Tissue tube graft at twelve months. The wall is much more compact and less cellular than at implantation. There is excellent endothelium denoted by the dark inner line. New fibrous tissue is well oriented and the fascia is intact. Hematoxylin and eosin, ×100.

B (No. 74-50), Tissue tube graft at fourteen months. This is much like *A* except that the new fibrous tissue is thicker and more compact, the fascia is very distinct, and a few hemosiderin deposits are seen beneath the endothelium. Hematoxylin and eosin, ×100.

an arterial graft. It is possible, of course, that raw fascial tubes could be used to bridge aortic defects since, in the aorta, the blood flow is turbulent and exerts a shearing action on irregularities of the wall. Such tubes were not successful, however, in several instances when tried during this study[2] and would not be expected to succeed in small arteries where flow is streamlined.

Fascial repair of arterial defects was reported by Herrick in 1918,[7] and fascial reinforcement of arteries and aorta has been described recently by several investigators. Arteries thinned by the Leriche stripping procedure may be successfully reinforced by a carefully sutured fascial layer.[23] In animals, arteries so reinforced did not rupture or become dilated. Thoracic aortic grafts constructed from fresh pericardium are described by Sako and associates.[18] When used alone, these tend to become dilated but, if they are reinforced with fascia, they maintain their shape well.[17] These combined pericardial-fascial grafts have characteristics similar to those of the tubes here reported. They have the advantage, if the heart is exposed, of being made and used immediately. This is an important piece of work and may well indicate a practical source for an autologous aortic graft when one is needed in the thorax.* Fascia consists mainly of strong collagen bundles, but it also contains fine elastic fibers which may in part account for its efficacy in arterial reinforcement (Fig. 4, *B*). Since the elastic tissue shows no definite increase or change in orientation even after a year, its precise role must remain conjecture only.

The possible value in man of the tissue tubes described in this paper lies in the treatment of nonemergency vascular lesions, such as aortic coarctation, aneurysm of the great vessels, and perhaps a few selected types of tumor, where adequate use of roentgenologic contrast methods would enable precise preoperative evaluation and point to the need of a graft. Preliminary studies suggest that it may also be possible to build tubes of any desired length in situ along the course of obliterative arterial lesions. If this proves to be the case, it is not unlikely that certain types of high-grade arterial insufficiency can be dealt with, without disturbing existing collaterals, by simple end-to-side anastomoses of the preformed tube at a second-stage operation. This might prove especially useful, since it appears that long homologous grafts of small caliber function for only a limited time and would, therefore, be unsuitable.[21]

SUMMARY

An experimental method for producing autologous tissue tubes to be used for aortic grafts is reported. The tubes consist of a fibroserous membrane resulting from reaction about a polyethylene tube implanted in the anterior rectus sheath of dogs plus a reinforcing fascial layer. The tubes require five to six weeks to produce and are thinner and harder to handle than actual arterial segments. When placed in the aorta to bridge a gap, however, they carry blood well, show no tendency to dilate, and do not undergo the degenerative changes common to all types of homologous grafts. Their possible use in human beings is discussed.

*A preliminary series of eight grafts using peritoneum suggests that this tissue is not suitable for the construction of arterial grafts.

REFERENCES

1. Carrel, A., and Guthrie, C. C.: Uniterminal and Biterminal Venous Transplantation, Surg., Gynec. & Obst. **2**: 266-286, 1906.
2. Dabbs, C. H.: Personal communication.
3. Deterling, R. A., Coleman, C. C., Jr., and Parshley, M. S.: Experimental Studies of the Frozen Homologous Aortic Graft, SURGERY **29**: 419-440, 1951.
4. Eastcott, H. G., and Hufnagel, C. A.: The Preservation of Arterial Grafts by Freezing, Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, 1950, Philadelphia, 1951, W. B. Saunders Company, pp. 269-274.
5. Gross, R. E.: Treatment of Certain Aortic Coarctations by Homologous Grafts: A Report of Nineteen Cases, Ann. Surg. **134**: 753-768, 1951.
6. Gross, R. E., Bill, A. H., Jr., and Peirce, E. C.: Methods for Preservation and Transplantation of Arterial Grafts. Observations on Arterial Grafts in Dogs. Report of Transplantation of Preserved Arterial Grafts in 9 Human Cases, Surg., Gynec. & Obst. **88**: 689-701, 1949.
7. Herrick, F. C.: An Experimental Study of Surgery of the Large Arteries: Aneurysm. The Placing of Musculofascial Inserts Within and Their Use in Patching Arteries, J. A. M. A. **71**: 2120-2122, 1918.
8. Johnson, J., Kirby, C. K., Greifenstein, F. E., and Gastello, A.: The Experimental and Clinical Use of Vein Grafts to Replace Defects of Large Arteries, SURGERY **26**: 945-956, 1949.
9. Keefer, E. B. C., Andrus, W. de W., Glenn, F., Humphreys, C. H., Lord, J. W., Jr., Murphy, W. B., and Tauroff, A. S. W.: The Blood Vessel Bank, J. A. M. A. **145**: 888-893, 1951.
10. McCune, W. S., and Blades, B.: The Viability of Long Blood Vessel Grafts, Ann. Surg. **134**: 769-781, 1951.
11. Miller, H. H., Callow, A. D., Welch, C. S., and MacMahon, H. E.: The Fate of Arterial Grafts in Small Arteries. An Experimental Study, Surg., Gynec. & Obst. **92**: 581-588, 1951.
12. Oudot, J.: La-greffe Vasculaire dans les Thromboses du Carrefour Aortique, Presse méd. **12**: 234-236, 1951.
13. Peirce, E. C., II.: Percutaneous Arterial Catheterization in Dogs With Special Reference to Aortography, Ann. Surg. **133**: 544-547, 1951.
14. Peirce, E. C., II.: Preservation of Endothelium in Refrigerated Aortic Segments and in Aortic Homografts in Dogs as Shown by Silver Staining, Anat. Rec. **112**: 831-842, 1952.
15. Peirce, E. C., II.: The Use of Viably Preserved Tissue for Homologous Arterial Grafts, Ann. Surg. **136**: 228-238, 1952.
16. Peirce, E. C., II., Rheinlander, H. F., Moritz, A. R., Gross, R. E., and Merrill, K., Jr.: Transplantation of Aortic Segments Fixed in 4 per cent Neutral Formalin. Report of Experiments in Dogs, Am. J. Surg. **48**: 314-323, 1949.
17. Sako, Y.: Prevention of Dilatation in Autogenous Venous and Pericardial Grafts in the Thoracic Aorta, SURGERY **30**: 148-160, 1951.
18. Sako, Y., Clatworthy, H. W., Chisholm, T., and Varco, R. L.: Observations on the Fate of Pericardial and Fascial Tissue Transplanted into the Thoracic Aorta. Abstract. Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, 1950, Philadelphia, 1951, W. B. Saunders Company, pp. 310-311.
19. Swan, H.: Some Observations on the Use of Arterial Homografts. Presented at Symposium on Blood Vessel Grafts, National Institutes of Health, Bethesda, Md., Jan. 10, 1952.
20. Swan, H., Robertson, H. T., and Johnson, M. E.: Arterial Homografts. I. The Fate of Preserved Aortic Grafts in the Dog, Surg., Gynec. & Obst. **90**: 568-579, 1950.
21. Welch, C. S.: Studies of the Function and Survival of Long Vascular Grafts. Presented at Symposium on Blood Vessel Grafts, National Institutes of Health, Bethesda, Md., Jan. 10, 1952.
22. Wheeldon, T.: The Use of Cellophane as a Permanent Tendon Sheath, J. Bone & Joint Surg. **21**: 393, 1939.
23. Wylie, E. J., Kerr, E., and Davies, O.: Experimental and Clinical Experiences With the Use of Fascia Lata Applied as a Graft About Major Arteries After Thrombo-endarterectomy and Aneurysmorrhaphy, Surg., Gynec. & Obst. **93**: 257-272, 1951.
24. Yeager, G. H., and Cowley, R. A.: Studies on the Use of Polythene as a Fibrous Tissue Stimulant, Ann. Surg. **128**: 509-520, 1948.

ABDOMINAL AORTIC ANEURYSM: RESECTION WITH PRESERVATION OF THE LUMEN

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ALTHOUGH aneurysms of peripheral arteries are considered to be serious, none are more serious or more life-threatening than those found in the aorta. In the past, they have been looked upon as a surgical "no man's land," where very few have attempted to tread. In the nineteenth century, surgeons who attacked this condition were, for the most part, looked upon with disfavor. Osler[1] stated that, in 1719, Valisneri of Padua was the first to report a surgical procedure upon an aneurysm. He was able to diagnose the pathology accurately, and a surgeon, who was not named, incised the mass with resultant fatal hemorrhage. In 1817, at Guy's Hospital in London, Astley Cooper first ligated the abdominal aorta for an iliofemoral aneurysm. The patient died within forty hours.[2] Since that time, numerous surgeons have ligated the aorta in the treatment of an aneurysm.

Aneurysms of the abdominal aorta are not as commonly encountered as one might suspect. In reviewing a series of one thousand aneurysms, Klotz found that six hundred ninety-five were arotic, and of these only eighty-five (12.2 per cent) were of the abdominal aorta.[3, 4] Etiologically, they may be placed into four groups: arteriosclerotic, syphilitic, mycotic, or traumatic. By far the most common in the abdominal portion is the arteriosclerotic, as opposed to the syphilitic being the most common in the thoracic aorta.

Since the first surgical attempt to correct this abnormality, many and varied procedures have been tried, and many of these have been abandoned for one reason or another. The successful procedures may be crystallized into three major types: (1) ligation of the aorta with or without excision of the aneurysm, (2) application of various chemical substances about the aneurysm to incite fibroplasia, (3) reconstruction or obliterative aneurysmorrhaphy as championed by Matas.[5]

The proponents of the ligation technique have felt that by occlusion of the aorta, the hemodynamics would be so altered as to reduce the pressure within the sac, and thereby prevent rupture. In theory this would be ideal, if it were not for the high mortality associated with the procedure. If the ligature is placed proximal to the renal arteries, death inevitably ensues from renal ischemia. Babcock[6] reports that in thirty ligations of the aorta below the renal arteries for aneurysms, only five patients survived, thus providing a mortality rate of 83.3 per cent. The most common cause of death is attributed to secondary hemorrhage which results from the ligature's cutting through the wall of the vessel

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and into the lumen. Silk, chromicized catgut, cotton, linen, cellophane, rubber bands, and metal bands have all been used. More success has been attained through the use of a wide ligature, which tends to minimize the cutting effect by distribution of pressure over a wider area. Aside from this complication, the operative shock of such a procedure accounts for some deaths. The application of a ligature is thought by some to produce a weakness of the wall and thereby predispose to secondary aneurysms.

Yeager and Cowley[7] have reported splendid results both experimentally and clinically in the use of polyethylene sheets impregnated with dicetyl phosphate as a fibrous stimulating agent. They make an excellent point in the careful selection of the polyethylene to be used as an onlay. The pure or inactive polyethylene is completely inert; on the other hand, the impure or reactive form (du Pont) contains 0.9 per cent dicetyl phosphate which is a potent sclerosing agent that stimulates fibroplasia. An important point in dealing with this product is to be absolutely sure of the specific type used if success is expected.

The observations of Matas on reconstructive or obliterative aneurysmorrhaphy are classical. This case report is a modification based upon his work. It is unfortunate that most abdominal aneurysms are of the fusiform rather than of the saccular variety. If the former is encountered, probably the method of Yeager and Cowley is the most efficacious. If they are of the latter type, it would seem that the technique set forth in this paper would be the one of choice.

Fig. 1.—Photograph showing large saccular aneurysm with area of anemic necrosis.

CASE REPORT

W. J. (University Hospital No. 56747), a 60-year-old Negro man, was admitted to the Vascular Service on March 20, 1952, with the chief complaint of severe abdominal pain, centered in a mass in the left lower quadrant. Present illness began in December, 1951, when he developed mild left lower quadrant pain associated with occasional bouts of nausea and vomiting. Upon massaging the abdomen, he stated that he felt a lump which was just below and to the left of the umbilicus. The mass steadily increased in size and the pain

became more severe, until on the night of admission it became so excruciating that he sought aid. He stated that about two days before admission, he noticed that the mass had suddenly grown much larger. For the past ten to fifteen years, he had noticed increasing throbbing pain in both legs with easy fatigability.

The review of symptoms and past history were essentially negative except for the fact that the patient had had a chronic productive cough for many years.

Physical examination showed the patient to be in excruciating pain. Temperature was 100° F., pulse 110, respirations 30 per minute, blood pressure 160/90. Chest examination revealed bilateral apical râles, both anteriorly and posteriorly, with diminution of breath sounds. Subsequent x-ray examinations and sputum studies revealed bilateral apical tuberculosis. The abdomen was tender to palpation throughout, but most marked in the left lower quadrant, where a mass about the size of an adult fist could be palpated. It was pulsating strongly. No bruit could be heard. The mass was easily movable superiorly and inferiorly, and appeared to be attached deeply. Femoral pulsations were present but diminished in intensity. The dorsalis pedis and posterior tibial arteries, bilaterally, could not be obtained. It was believed that an aneurysm of the abdominal aorta existed with impending perforation.

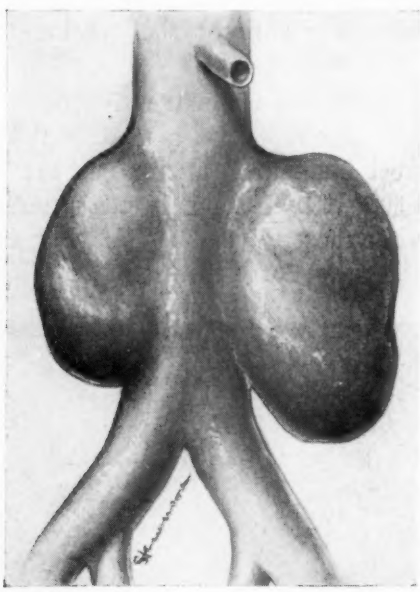

Fig. 2.—Sketch showing relationship of saccular and fusiform aneurysm to aorta and its bifurcation.

Under cyclopropane endotracheal anesthesia, the abdomen was opened through a left rectus incision. The small bowel was displaced superiorly and to the right. Protruding upward from the left, arising from the aorta in the region of the fourth lumbar vertebra, was a large pulsating mass measuring 10 by 5.5 by 5.5 cm. This mass represented a large saccular aneurysm arising from the left side of a fusiform aneurysm of the abdominal aorta. The thin-walled saccular aneurysm presented areas of recent secondary sacculations, as well as an area of anemic necrosis measuring approximately 1 cm. in diameter. There were areas of cholesterol degeneration. The saccular portion of the aneurysm presented a picture of imminent rupture (Figs. 1 and 2).

The peritoneum over the aneurysm was incised and reflected from the abdominal aorta. A fusiform dilatation of the aorta was uncovered with a minor saccular extension from the right and a major extension from the left, as previously described (Fig. 2). The decision to excise the saccular aneurysm and to onlay the fusiform aneurysm with polyethylene was made. The aorta proximal to the aneurysm and the common iliacs distally were isolated, and wide cotton tapes were placed around each site. These tapes were used to

maintain temporary occlusion, both proximal and distal to the operative site, parallel to the aorta. A small cuff was left for closure (Fig. 3, *left*). The sac was filled with a large, extremely soft and friable laminated clot (Fig. 4).

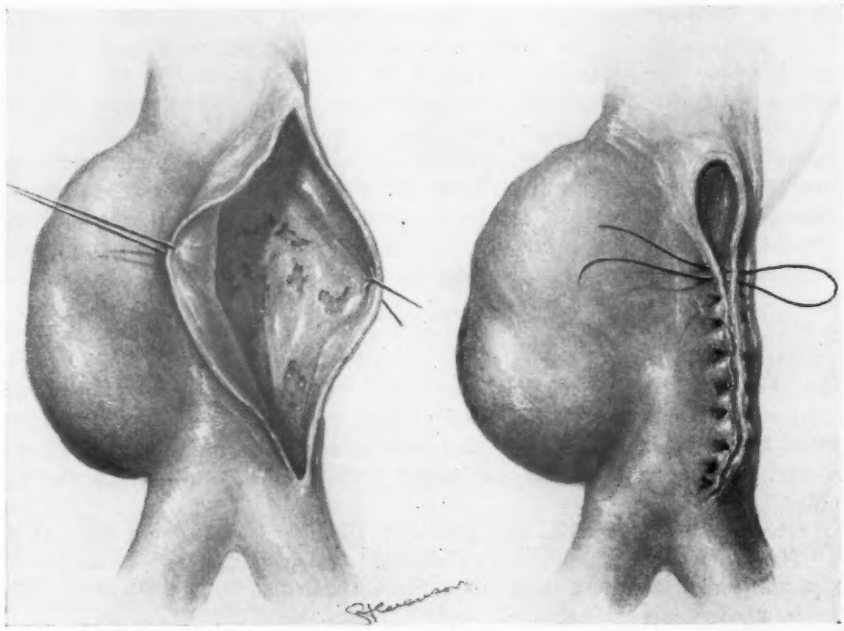

Fig. 3.—*Left*, Sketch showing saccular aneurysm excised, leaving a small cuff for closure. Ulcerated arteriosclerotic plaques are noted, involving the intima.
Right, Sketch showing method of closure of resultant aortic defect.

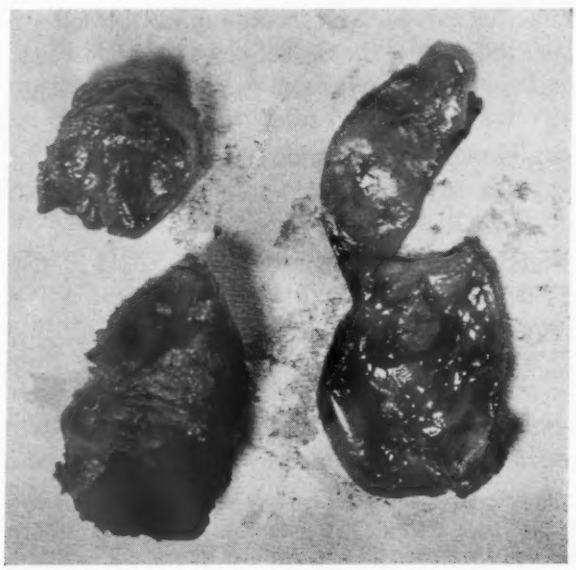

Fig. 4.—Photograph showing excised sac and soft laminated thrombus.

A thrombus was also present in the fusiform aneurysm. This was evacuated, and the pouch was irrigated with saline and heparin. The intima of the aorta showed marked atheromatous changes with large ulcerated plaques (Fig. 3, *left*). The defect on the left side of the aorta, which now measured 7.5 cm. in length, was closed with interrupted hori-

zontal mattress sutures of 000 black silk, which everted the intima (Fig. 3, *right*). A second reinforcing layer secured the closure. The temporary occluding tapes about the iliacs were slowly removed, following which the tape occluding the proximal aorta was released. No leaks within the suture line were noted. A large sheet of reactive polyethylene was then placed over the fusiform aneurysm and the suture line. This was firmly secured to the serosa of the posterior wall of the aorta with 000 black silk sutures. A section from a one-inch slingshot rubber band was placed around the proximal aorta. It was pulled taut and sutured with an estimated 25 per cent compression of the aorta. The abdomen was then closed in layers, using No. 32 stainless steel wire.

Postoperative Course.—Immediately following the operation no pulsations could be felt in the dorsalis pedis or posterior tibial arteries. Continuous heparinization was maintained and Dicumarol therapy initiated. As Dicumarolization was effected, the heparin was discontinued. Penicillin was given in 400,000 unit doses twice daily for five days. Tetraethylammonium chloride, 400 mg. intramuscularly, was also given. This was discontinued because of an adverse effect on the blood pressure. Twenty-four hours after surgery, the temperature spiked to 103.6° F., but returned to normal on the third postoperative day, and remained so until the patient's discharge. Twelve hours after surgery, good, full, bounding pulses were felt in the dorsalis pedis and posterior tibial arteries. The patient was ambulant by the third day; he stated that the pain which had been present in his legs for the past ten to fifteen years had completely disappeared. Skin sutures were removed on the ninth postoperative day, and the patient was discharged from the hospital on the thirteenth postoperative day.

The femoral, dorsalis pedis, and posterior tibial pulses in both legs and feet are excellent. The patient has absolutely no abdominal or leg pain. He was last seen on April 24, 1952, pending admission to a tuberculosis sanatorium.

SUMMARY AND CONCLUSION

1. A brief history of abdominal aortic aneurysms has been presented with a short discussion of the various methods of treatment.

2. A case is presented in which a saccular dilatation of a fusiform abdominal aortic aneurysm was excised and the defect closed with preservation of the aortic lumen. The residual fusiform aneurysm was treated with an onlay of polyethylene.

3. All cases of abdominal arotic aneurysm are deserving of an attempt at definitive therapy.

ADDENDUM

Since the completion of this paper, a fusiform aneurysm of the abdominal aorta has also been successfully treated by the described method. A report on this is forthcoming.

Acknowledgment.—The authors wish to extend their appreciation to Mr. Thomas Stevenson and Mr. Ray Clayton of the Department of Art, University of Maryland School of Medicine, for their aid in the preparation of the drawings and photographs used in this paper.

REFERENCES

1. Osler, W.: Aneurysm of the Abdominal Aorta, Lancet **2**: 1089, 1905.
2. Croot, H. J.: Ligation of the Aorta and the Use of Cellophane for Abdominal Aneurysm, Brit. J. Surg. **38**: 432, 1950-1951.
3. Klotz, O.: Concerning Aneurysms. Third Gordon Bell Memorial Lecture, Toronto, 1926, University of Toronto Press.
4. Hirschowitz, B. I., and Bagg, L.: Aneurysms of the Abdominal Aorta With a Report of Four Unusual Cases, Gastroenterology **18**: 361, 1951.
5. Matas, R.: An Operation for the Radical Cure of Aneurysm Based Upon Arteriorrhaphy, Tr. Am. S. A. **20**: 396, 1902.
6. Babcock, W. W.: The Surgical Treatment of Aortic Aneurysms, South. M. J. 43: 23, 1950.
7. Yeager, G. H., and Cowley, R. A.: Studies on the Use of Polythene as a Fibrous Tissue Stimulant, Ann. Surg. **128**: 509, 1948.

LIGATION OF THE HEPATIC AND SPLENIC ARTERIES FOR ADVANCED PERIPORTAL CIRRHOSIS

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ACCORDING to Patek[1] one-third of all patients with portal cirrhosis under medical treatment will have hematemesis, and of these only 50 per cent will be alive at the end of one year. This observation, coupled with the fact that of those who bleed from esophageal varices 20 per cent will die with their first hemorrhage, emphasizes the necessity for some dependable form of treatment. It is only in relatively recent times that much has been done about this problem, but considerable data have accumulated during the past decade.

Increased venous pressure within the portal system has come to be known as portal hypertension. The blockage of the portal flow may occur within the portal vein and its major tributaries, or it may occur within the liver. It has been estimated that 75 per cent of cases are due to the intrahepatic blockage which accompanies Laennec's cirrhosis. Of all blood passing through the liver about 75 per cent is contributed by the portal vein and 25 per cent by the hepatic artery. The flow from each source eventually reaches the same sinusoids where there is an equalization of pressure. The normal range of pressure within the portal system is 100 to 150 mm. of water. In portal hypertension the pressures may reach as high as 600 mm. of water. There is no obvious correlation between portal pressures and severity of symptoms.

Efforts to reduce abnormally high portal pressures can be classified generally into two groups: the first concerns itself primarily with reducing the amount of blood flowing through the portal system by means of arterial ligations; the second method attempts to produce an equalization between a normal systemic pressure and a high portal pressure by means of venous shunts.

Much outstanding work has been done by Blakemore, Lord, Linton, Whipple, Julian, Hardy, Smith, Freeman, Thorek, and many others on the various shunt operations. The mortality rate has been greatly reduced, but the fact remains that these short-circuiting operations are of necessity long and tedious procedures which place a heavy load on poor-risk patients. Arterial ligations are much easier to accomplish from a technical standpoint and are less time consuming. A. W. Blain[2] reported a case of ligation of the splenic artery for Banti's disease in 1918 and again in 1950 in conjunction with Blain, III.[3] For years sporadic reports appeared. It remained, however, for Rienhoff and Berman to reawaken interest in this subject, and at the present time there is considerable work being done in various parts of the country.

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Hemorrhage from esophageal varices is the alarming complication of portal hypertension which usually stimulates a surgical approach to the problem. Less dramatic, but also very distressing, is severe ascites. Both of these complications will respond to anything which effectively lowers the portal tension.

Rienhoff[4] postulates that the pressure within the portal vein is definitely lowered when the hepatic artery is ligated, and that this pressure can be still further lowered by ligation of the splenic artery. It is a known fact that 30 per cent of the blood carried by the portal vein is contributed by the spleen, and it would follow, therefore, that diminishing the splenic flow would reduce the portal flow. There is good evidence that simple ligation of the splenic artery in these cases is superior to splenectomy by virtue of preserving some naturally developed venous collaterals. As previously noted, 25 per cent of the blood passing through the liver is brought by the hepatic artery. The arterial pressure is 10 to 12 times greater than the portal pressure. These two pressures apparently compete for dominance in the sinusoids. When the resistance to arterial flow is diminished, as occurs in cirrhosis, the resistance to portal flow is proportionately increased. From this is derived the rationale that lowering the arterial pressure by ligation also lowers that in the portal vein.

The first operation in which both the hepatic and splenic arteries were ligated by Rienhoff was performed for ascites; the second was for exsanguinating hemorrhage. These patients underwent operations in 1947 and 1950, respectively, and are alive and well at this date, without having had recurrence of complications. In all, Rienhoff[5] has collected 70 case reports, of which 15 were those of patients he had operated upon personally. There was one death in his personal series, which he did not believe was due to liver damage, although no autopsy was performed. He recommended that the splenic artery be ligated close to the celiac axis and that the hepatic artery be ligated just distal to the departure of the gastroduodenal branch. He emphasized the importance of protecting the liver by giving large doses of penicillin and streptomycin for a week pre- and postoperatively. Berman,[6] on the other hand, felt that there was a great danger of liver necrosis by occluding the hepatic artery at this point and advised ligation close to the celiac axis so as to allow some collateral circulation to come through the gastroduodenal artery. Acting on the evidence provided by Brown and Derr[7] that the gastric arteries continue to fill in spite of ligation of all branches of the celiac axis, Berman has recently been ligating the left gastric artery in addition to the hepatic and splenic arteries. He stated, "There is a fall in pressure of the coronary vein following this procedure which may be of great importance when esophageal varices are present." Thorek[8] ligates the splenic and hepatic vessels close to the celiac axis.

Changes in portal pressure can be demonstrated by inserting a needle into one of the veins which is tributary to the portal system and attaching this to a manometer. Readings taken before and after the vessels are occluded will usually demonstrate a marked reduction in pressure. The manometer (Fig. 1)

is a simple device calibrated in millimeters. It can be readily made in any laboratory. During use, the system is filled with saline or citrate solution and the zero mark must be held at the level of the portal vein. Readings are made directly from the top of the column.

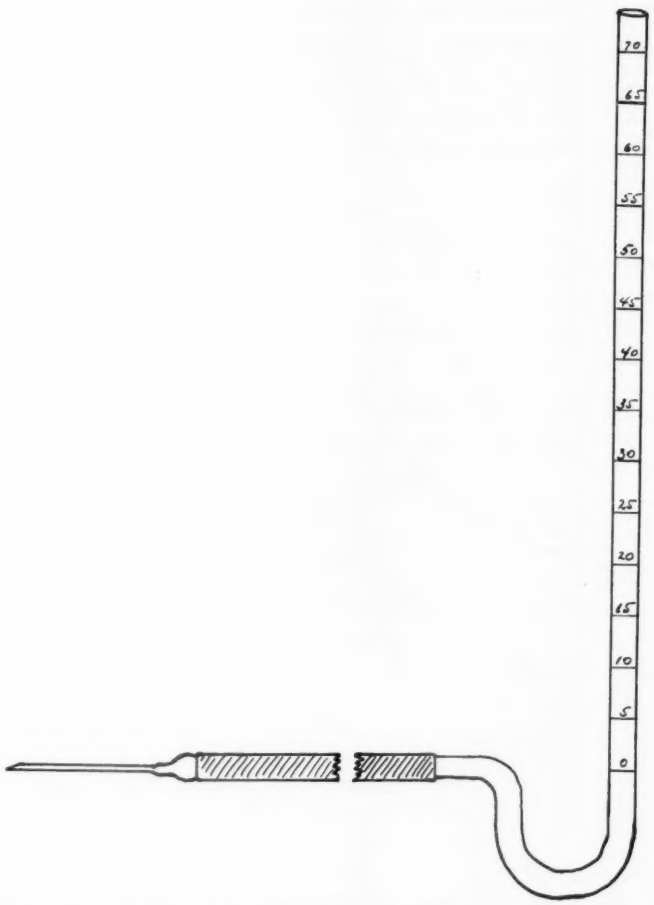

Fig. 1.—Simple glass manometer with rubber tubing and needle attached. For convenience in representation the calibration is in centimeters but actual readings are made in millimeters. The system is completely filled with citrate solution before introducing the needle into a portal tributary.

Attention is directed to Fig. 2 for a brief review of the ramifications of the celiac axis. The latter is a short trunk about 1 cm. in length and 1 cm. in diameter which arises from the anterior surface of the aorta at the level of the first lumbar vertebra just above the superior aspect of the body of the pancreas. It is most easily approached through a rent in the gastrohepatic omentum, or it can be exposed by incising the great omentum along the greater curvature of the stomach and by elevating the latter organ. The pulsation is strong and can be felt just above the pancreas. Caution is recommended upon incising the peritoneum over the vessel because the adipose areolar tissue in which it lies buried has an abundant supply of small arteries and thin-walled veins which bleed briskly when torn and rapidly obscure the field. The splenic

branch tends to dip immediately into the substance of the pancreas and often lends itself more readily to ligation at a point 5 to 7 cm. to the left where it reappears along the superior border of the pancreas. The hepatic artery can be ligated near its parent trunk or can be traced to the right until the gastroduodenal branch is seen to come off at nearly a right angle from the inferior surface. Occasionally the gastroduodenal branch is larger than the hepatic artery distal to this point. The left gastric artery can be exposed and ligated just above the celiac axis. In general, ligation in continuity with heavy silk is preferable to division of these large vessels. Anastomoses with the esophageal, inferior phrenic, and inferior pancreaticoduoduenal arteries are indicated in the diagram.

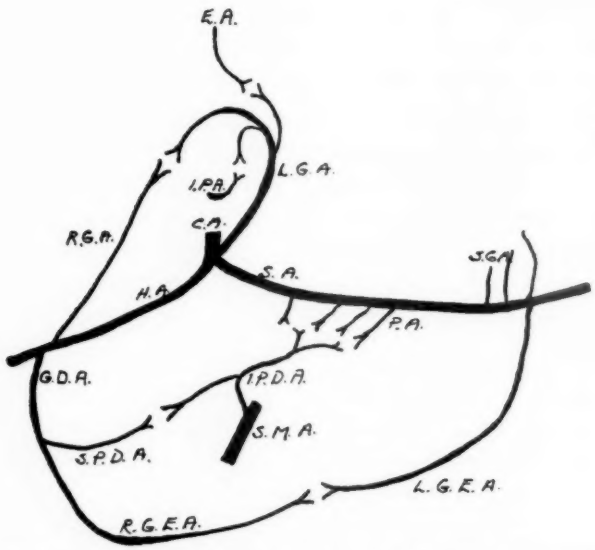

Fig. 2.—Schematic representation of celiac axis with main anastomotic areas indicated by forking branches. Points of ligation are not indicated but will be immediately apparent. C.A.—celiac axis, R.G.A.—right gastric artery, L.G.A.—left gastric artery, H.A.—hepatic artery, S.A.—splenic artery, G.D.A.—gastroduodenal artery, S.P.D.A. superior pancreaticoduodenal artery, I.P.D.A.—inferior pancreaticoduodenal artery, S.M.A.—superior mesenteric artery, R.G.E.A.—right gastroepiploic artery, L.G.E.A.—left gastroepiploic artery, S.G.A.—short gastric arteries, P.A.—pancreatic branches from splenic artery, I.P.A.—inferior phrenic artery, E.A.—esophageal artery.

CASE REPORTS

CASE 1.—G. H., a 66-year-old white man, was first admitted to the Highland Park General Hospital on May 28, 1951, because of bloody vomitus and tarry stools. The patient stated that he had been fairly well until about five weeks previously when he first noticed crampy abdominal pain associated with flatulence and vague indigestion. These manifestations continued until five days prior to admission when he vomited a copious amount of coffee-ground material. Shortly thereafter he began to have tarry stools. Review of the past history revealed that the patient had consumed from eight to sixteen ounces of whisky daily for several years. He stated that prior to this he had drunk very heavily. He was treated for pulmonary tuberculosis in 1929. No food idiosyncrasies can be elicited. There was no history of jaundice, clay-colored stools, or dark urine. He denied the use of tobacco or drugs, and stated that he had always been inclined to be thin and nervous.

Examination.—Physical examination revealed a pale, apprehensive, elderly, white man in no pain or respiratory distress. The temperature was 98.6° F., pulse 100, blood pressure 122/80. The skin was slightly jaundiced. Findings referable to the head and neck were non-

contributory. Heart sounds were regular and of good quality. No murmurs were noted. The abdomen presented no scars, masses, or tenderness. The liver, spleen, and kidneys were not palpable. An easily reducible, large, complete, inguinal hernia was present. Rectal examination was negative. The back and spine were not remarkable. Blood studies were as follows: Hemoglobin 33 per cent, red blood count 1,900,000, white blood count 5,700, polymorphonuclears 87 per cent, lymphocytes 12 per cent, monocytes 1 per cent. Serology was negative. Urinalysis was negative. X-ray studies revealed a healed, inactive, acid-fast lesion involving both upper lung fields. There was evidence of a large diaphragmatic hernia containing the upper portion of the stomach. There was also evidence of varicosities in the lower esophagus. Areas of increased density were present in the upper right quadrant and were thought to be gallstone shadows. In addition, there was extensive diverticulosis of the colon with considerable irritability of the sigmoid area.

Course.—Gastrointestinal bleeding stopped spontaneously. The patient was given several transfusions and was sent home under appropriate medical management. The tentative diagnosis was cirrhosis of the liver with hemorrhage from esophageal varices.

Second Admission.—The patient was readmitted to the hospital on June 11, 1951. He had been well until the day of admission when he had a massive emesis of both bright and dark blood and had also passed tarry stools. Examination at this time revealed him to be markedly exsanguinated. Blood pressure was 100/60, pulse 120, hemoglobin less than 40 per cent, red blood count 1,500,000. In spite of all therapy, the patient continued to hemorrhage actively, and he was in a state of circulatory shock for several days. Blood was given constantly in two extremities. A Patton tube was ineffective, possibly because of the presence of the diaphragmatic hernia. Gelfoam and topical thrombin were likewise of no avail. A total of 16,000 c.c. of blood was given. At no time during the critical stage was the patient's condition such that surgery could be contemplated. He finally stopped bleeding spontaneously, following which his condition improved rapidly. He was permitted to leave the hospital on July 1, 1951, for further convalescence at home. It was felt that some type of surgery should be undertaken as soon as his condition would permit.

Third Admission.—The patient was readmitted on Aug. 15, 1951, in good general condition. He stated that he had gained weight, had had an excellent appetite, and had experienced no further bleeding. Examination revealed the following salient points: blood pressure 120/80, pulse 80, hemoglobin 78 per cent, red blood count 3,900,000, white blood count 4,100, cephalin cholesterol flocculation 4 plus, total serum proteins 6.0 mg., serum albumin 3.6 mg., serum globulin 2.4 mg.

For one week prior to admission the patient had been given 400,000 units of penicillin daily. After admission he was given 50,000 units of penicillin and 0.25 Gm. of streptomycin every four hours before and after surgery.

Operation.—The patient was taken to the operating room on Aug. 16, 1951. Anesthesia consisted of a combination of pentothal, curare, nitrous oxide-oxygen, and intravenous procaine. Through a midline upper abdominal incision the abdomen was explored. Gentle palpation confirmed the presence of a diaphragmatic hernia which contained the upper one-third of the stomach. The liver was slightly enlarged and presented a typical hobnail appearance. The gall bladder contained many stones. There was no evidence of duodenal ulceration. The spleen was somewhat enlarged. The celiac axis was exposed by dividing the gastrohepatic ligament and incising the posterior peritoneum. Many small retroperitoneal varices were present. A silk ligature was passed around the splenic artery close to the celiac axis but was not tied. The hepatic artery was identified and traced distally until the gastroduodenal artery was encountered. An untied ligature was then placed around the hepatic artery just distal to this point. A rather large tributary to the portal vein was then selected in this area and a needle connected to a manometer was introduced into the vein. The pressure was recorded as 220 mm. of water with the manometer at the level of the portal vein. The splenic and hepatic arteries were then doubly ligated in continuity with heavy silk and the pressure promptly fell to 130 mm. of water. A liver biopsy was taken and the wound was closed.

Pathology.—The biopsy revealed typical Laennec's cirrhosis with active periportal inflammation.

Postoperative Course.—Penicillin and streptomycin were given for one week postoperatively. The patient became ambulatory on the first postoperative day. At no time was the temperature above normal. He made an uneventful recovery and left the hospital on Aug. 25, 1951.

Follow-up.—During the ten months since surgery, the patient has been in exceptionally good health and spirits. He is working regularly and states that he has not felt better in years. He has been free of indigestion and upper abdominal distress. There has been no recurrence of hematemesis or tarry stools.

CASE 2.—P. R., a 55-year-old white man, was admitted to the Highland Park General Hospital on Sept. 5, 1951, with a chief complaint of enlargement of the abdomen. He stated that he had been in good general health until about one year previously when he began to notice sluggishness, poor appetite, and weight loss. In spite of these manifestations, his abdomen increased in size. By May, 1951, his girth had become so great that he was extremely uncomfortable. He stated there was also marked swelling of his legs and genitalia. Questioning revealed that he first had consulted an osteopathic physician who diagnosed the condition as cirrhosis but recommended no treatment.

In July, 1951, the patient presented himself at the office of the senior author (J. A. W.). A summary of the office record yielded the following pertinent information: "A paracentesis was performed and approximately two gallons of cloudy, yellow fluid were removed. Palpation of the abdomen afterward revealed a large, firm, nodular mass occupying the upper right quadrant and extending into the upper left quadrant. The lower border was approximately level with the anterior superior iliac spine. The mass moved with respiration and was not tender. The symptoms were completely relieved and the swelling disappeared from the lower extremities. Within ten days the fluid had reaccumulated and the associated manifestations had recurred. It became necessary to perform a paracentesis at approximately ten day intervals. Mercurial diuretics were not effective. After two months of this treatment the patient's general condition was deteriorating so rapidly due to constant loss of protein in the ascitic fluid that he realized the grave portent of his disease and demanded that something be done. He was advised of a few reported cases of ascites due to cirrhosis, in which ligation of the hepatic and splenic arteries had stopped further fluid formation, but was cautioned that this treatment was still in its experimental stages. It was his wish that this operation be performed."

Further review of the past history was essentially noncontributory except to show that the patient had been a heavy drinker all his life—consuming usually in excess of one quart of whisky daily.

Examination.—The patient presented evidence of weight loss and dehydration. The skin was dry and lacked turgor but was not jaundiced. Dental hygiene was poor. Blood pressure was 116/80. The lungs were clear. Heart sounds were regular and of fair quality; no murmurs were audible. The abdomen presented marked enlargement with shifting dullness and dilated superficial veins. An easily reducible right inguinal hernia was present. There was marked pitting edema of the scrotum and both lower extremities. Blood studies were as follows: hemoglobin 80 per cent, red blood count 4,200,000, white blood count 8,300, polymorphonuclears 72 per cent, lymphocytes 23 per cent, monocytes 4 per cent, eosinophiles 1 per cent. Serology was negative. Prothrombin time was 100 per cent of normal. Other tests showed: total serum proteins 5 Gm., serum albumin 2.5 mg., serum globulin 2.5 Gm., nonprotein nitrogen 30 mg., sugar 80 mg., cephalin cholesterol floculation 3 plus. Urinalysis was albumin negative, sugar negative. Sediment showed an occasional white cell. A diagnosis of cirrhosis of the liver with ascites was made and the patient was prepared for surgery.

Operation.—The patient underwent surgery on Sept. 7, 1951. Anesthesia consisted of pentothal, curare, nitrous oxide-oxygen, and intravenous procaine. An upper midline in-

cision was made. A large amount of cloudy, yellow ascitic fluid was aspirated. There were many adhesions between the omentum and the anterior abdominal wall which contained large veins. These adhesions were not divided. The veins in the falciform ligament were also greatly enlarged. The liver was markedly enlarged, nodular, and typically hobnailed in appearance. The stomach presented dilated veins on its serosal surface, especially in the region of the esophagus. The remainder of the exploratory examination was essentially negative. There was no appreciable thickening or frosting of the peritoneal surfaces. An incision was made in the gastrohepatic ligament and in the posterior wall of the bursa omentalis in the region of the celiac axis. Exposure of this arterial trunk was made extremely difficult by huge dilated veins in this area. It was noted that the ascitic fluid accumulated constantly and was always a factor in obscuring the operative field. An untied ligature was placed around the splenic artery immediately distal to the celiac axis and a second untied ligature was passed around the hepatic artery just distal to the departure of the gastroduodenal artery. Portal pressures were then taken by inserting a needle into one of the large omental veins. The pressure was found to be 260 mm. of water. Following this the ligatures were tied, and a second reading revealed no change in portal pressure. In an attempt to further decrease the amount of blood going to the liver, the hepatic artery was temporarily occluded by pressure proximal to the gastroduodenal artery. This resulted in a slight reduction to 220 mm. of water. A permanent ligature was then also applied in this position. The color of the stomach remained good. A biopsy of the liver was taken and the abdominal wall was closed around two large cigarette drains.

Pathologic Diagnosis.—The disease was diagnosed as advanced portal cirrhosis of the liver with areas showing central necrosis.

Postoperative Course.—The patient's general condition seemed good for approximately thirty-six hours. It was noted that there was very scant drainage of ascitic fluid on the dressings. On the second postoperative day the patient complained of sudden weakness and a feeling of abdominal pressure; objectively he appeared pale and the abdomen was distended. Twelve hours later he began to vomit huge amounts of coffee-ground material. He became mentally confused, persistently pulled out his Levin tube, and picked aimlessly at the bedclothes. From this point his condition rapidly deteriorated and he became extremely noisy and uncooperative. Blood nonprotein nitrogen was 125 mg. and the urea nitrogen was 87 mg. Serum chlorides were within normal limits. On September 11, four days postoperatively, his condition became critical and he died at 4:00 P.M.

Autopsy.—A post-mortem examination was conducted within two hours after death. No appreciable amount of ascitic fluid had accumulated within the peritoneal cavity. The entire intestinal tract was distended with a huge amount of blood, the source of which was found to be large varices at the esophagogastric junction. It was surmised that the terminal uremia was due to absorption of large amounts of nitrogen from the blood in the intestinal tract. The liver appeared more mottled than previously but neither it nor the spleen were infarcted grossly or microscopically. The ligation of the hepatic and splenic arteries was verified. The portal vein presented no gross abnormality. The gastric wall presented several small superficial terminal ulcerations but was otherwise negative.

Final Diagnosis.—The condition was diagnosed as periportal cirrhosis of the liver complicated by massive intragastric hemorrhage from associated varices.

EXPERIMENTAL STUDIES

The unexpected fatal hemorrhage in Case 2 gave rise to considerable speculation as to why there should have been esophageal bleeding in a patient who had had none previously, especially immediately following an operation designed to avoid it! We recalled that Berman had postulated a fall in coronary venous pressure when the left gastric artery was divided and conjectured

whether the reverse condition could obtain, for example, an increase in the coronary venous pressure following an increase in pressure in the left gastric artery. The problem then was to determine whether the pressure in the left gastric artery was altered by occlusion of the hepatic and splenic arteries. We could find no reference in the literature to give us a clue, so the following experiment was set up using healthy adult dogs weighing between 40 and 50 pounds. Standard veterinary pentobarbital solution was used intravenously for anesthesia on the basis of 1 c.c. per 5 pounds of body weight.

Method.—The celiac axis and its three major branches were identified, and traction sutures were passed under them. The left gastric artery was divided 2 cm. from the axis and an 18 gauge cannula was inserted into the proximal end. The stilette was withdrawn and a mercury manometer with its connecting tubing filled with citrate solution was attached. A direct blood pressure reading was taken. The hepatic and splenic arteries were then occluded with bulldog clamps and a second reading was made. The clamps were released and, after more citrate was injected through the wall of the rubber tubing to prevent clotting in the system, the readings were repeated.

Results.—Because the results were so consistent the series is short. Our findings are summarized in Table I.

TABLE I. RESPONSE OF PRESSURE IN LEFT GASTRIC ARTERY TO OCCLUSION OF HEPATIC AND SPLENIC ARTERIES*

DOG	BEFORE OCCLUSION		AFTER OCCLUSION	
	FIRST READING	SECOND READING	FIRST READING	SECOND READING
1	160	156	170	170
2	156	154	168	170
3	140	140	160	162

We believe that the small rise in blood pressure in the left gastric artery following occlusion of the hepatic and splenic arteries is significant and may possibly account for the esophageal hemorrhage in Case 2. It must be remembered that this patient sustained practically no reduction of portal pressure following hepatic and splenic artery ligations, and, in the light of these findings, may even have been subjected to an increase in pressure in the coronary and esophageal veins.

COMMENT

As with any relatively new procedure, evaluation is difficult. It would appear that one potential weakness is the development over a period of time of a collateral arterial supply which nearly equals the original. We must also take into consideration the possibility of the presence of arterial anomalies. Occasionally the right hepatic artery arises from the aorta, superior mesenteric, or right renal arteries. An accessory hepatic artery may arise from the superior mesenteric artery[7] and, in such cases, it will almost certainly be overlooked. Instances of the left hepatic artery arising from the left gastric artery have been reported.[9] We have personally observed upon several occasions a large accessory hepatic artery arising from the beginning of the left

gastric artery and traversing the superior portion of the gastrohepatic ligament to terminate in the porta hepatis. Arteriography can anticipate much of this for us.

Although we have a mortality rate of 50 per cent in our cases we are not discouraged about the possible benefits of the procedure. It must be remembered that the operation is recommended only in advanced cases of cirrhosis in which the afflicted individuals have less than a year of life expectancy. Marked ascites generally indicates poor operative risk, as was borne out in our second case, although Berman and Rienhoff have had some of their most satisfactory results in such instances. It is difficult to determine why there was no diminution of portal pressure in Case 2 after such extensive ligation. Possibly the arterial blood was already being completely shunted away from the liver sinusoids as a result of the advanced cirrhosis and was emptying directly into the central hepatic veins. We can only speculate whether additional ligation of the left gastric artery would have lowered the pressure in the coronary vein sufficiently to have averted the fatal hemorrhage which ensued. Our experimental findings suggest that this should have been done. While it must be remembered that our experiments were carried out on normal anesthetized dogs it would seem likely that the hemodynamics would be comparable to those encountered in human beings. In order to avoid the risk of increasing the pressure in the left gastric artery after ligation of the splenic and hepatic arteries has been accomplished, we feel that all three of the branches of the celiac axis should be ligated close to the parent trunk. Before actual ligation is carried out, however, the portal pressure should be read, after producing a temporary occlusion with soft-jawed clamps. If no drop in portal pressure is encountered a careful search should be made for anomalous vessels. If this fails, the ligation should be abandoned and a shunt procedure carried out, provided the patient's condition warrants such treatment.

SUMMARY

Portal hypertension in the majority of cases is due to the intrahepatic blockage which accompanies Laennec's cirrhosis. It can be demonstrated by manometric readings that the portal pressure is markedly reduced in some of these cases by ligation of the splenic and hepatic arteries. Such ligations are technically easier to accomplish and are less time consuming than venous shunts.

Animal experiments suggest that ligation of the splenic and hepatic arteries results in a slight to moderate increase of pressure within the left gastric artery.

Methods of surgical approach to the celiac axis are discussed. Arterial anomalies are considered briefly. A simple manometer for determining portal pressures is described. Two cases are presented.

ADDENDUM

Since this article was submitted for publication we have had one additional case of hemorrhage from esophageal varices due to cirrhosis which was treated by ligation. In this case occlusion of all three branches of the celiac axis produced a pressure drop from

320 mm. of water to 230 mm. of water. This was regarded as favorable and the vessels were permanently ligated close to the parent trunk. The patient, four months postoperatively, has had no recurrent hemorrhage and states that she is feeling very well.

We are indebted to the Department of Research of Harper Hospital for the privilege of using the facilities of their dog laboratory, and to Dr. James E. Cole for his assistance and advice.

REFERENCES

1. Patek, A. J., Jr.: Portacaval Shunt for Portal Hypertension, J. A. M. A. **145**: 1335-1339, 1951.
2. Blain, A. W.: Ligation of the Splenic Artery for Banti's Disease. Report of a Case, Experimental Studies, Surg., Gynec. & Obst. **26**: 660, 1918.
3. Blain, A. W., and Blain, A., III: Ligation of the Splenic Artery, the Operation of Choice in Selected Cases of Portal Hypertension and Banti's Syndrome, Ann. Surg. **131**: 92, 1950.
4. Rienhoff, W. J., Jr.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension With a Report of Six Cases, Preliminary Report, Bull. Johns Hopkins Hosp. **88**: 368, 1951.
5. Rienhoff, W. J., Jr.: Personal communication, Jan. 3, 1950.
6. Berman, J. K.: Personal communication, Dec. 14, 1951.
7. Brown, J. R., and Derr, W.: Arterial Blood Supply of the Human Stomach, Arch. Surg. **64**: 616-621, 1952.
8. Thorek, P.: Personal communication, Oct. 10, 1951.
9. Anson, Barry J.: Atlas of Human Anatomy, Philadelphia, 1950, W. B. Saunders Company, p. 303.

THE EXPOSURE METHOD IN THE TREATMENT OF SEVERE SECOND AND THIRD DEGREE BURNS

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IN AN appraisal of current thought on the local treatment of severe burns, it is generally accepted that the most orthodox and universally practiced treatment is the so-called closed or occlusive dressing. This has been used in one form or another from time immemorial, but popularized and modernized in this country by Allen and Koch.[1] This type of local therapy is the sequel to the chemical or dye methods used in the previous decade.

With reference to the systemic therapy of burns, certain well-established principles have been agreed upon in recent years. It is not within the purview of this short essay to dilate on the accepted tenets of supportive therapy.

The closed, or occlusive, dressing treatment has proved very satisfactory in civilian and military practice to date and has been amply substantiated in careful studies by Allen and Koch,[1] Siler and Reid,[2] Cope,[3] and Evans,[4] in this country, and by Colebrook[5] and Bull,[6] in England. However, with the possible impact of atomic disaster and the inevitable mass casualties, most of the required surgical steps of the closed therapy of burns become impossible of attainment. We may quickly grasp the magnitude of this problem in terms of expected burn casualties following an atomic blast when we realize that in a single atomic explosion, such as occurred at Hiroshima, approximately 34,000 serious burn wounds were inflicted. Pearse has graphically depicted the staggering personnel and equipment needed to treat these patients, using our present standardized techniques. He estimated that for 34,000 patients, 170,000 professional persons, and 8,000 tons of equipment would be needed.[7]

The virtual impossibility of using the closed-dressing system in the management of burns reaching such astronomical numbers is apparent, and for the following reasons: (1) There is a definite shortage of trained personnel to apply properly the initial and subsequent time-consuming dressings, and to administer fluids, oxygen, and anesthesia when needed for such dressings, (2) the cost of manufacture and strategic storage of dressing materials in the vast quantities needed, is tremendous, and (3) available professional and nursing care cannot be disproportionately used on burn casualties as against the needs of other traumatic casualties.

The exposure treatment is not new, having been briefly described by Copeland[8] in 1887, more extensively by Sneve[9] in 1905, and again in 1915 by Haas.[10]

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It is difficult to understand the abandonment of the exposure method at that time, since a review of published reports on both exposure and closed types of treatment as practiced in that era showed a comparable morbidity and mortality.[10] Then followed a thirty-year period of disuse until its revival by Wallace[11] of Edinburgh in 1947. The exposure form of treatment may be simply defined as the exposure of the burn wound to the open air at room temperature. Certain limitations of this oversimplified definition will be discussed and, of course, they represent significant changes over the technique used by the early originators.

In summary, the goal sought is a type of local burn therapy which will be simpler than the closed method, and productive of equal or better results when applied to the handling of mass casualties. In an effort to achieve a possible solution to this problem, we, on the Surgical Service of St. Vincent's Hospital, following the initial work of Wallace and, recently, of Pulaski,[12, 13] Blocker,[14] and Artz[15] in this country, and with the active support of the Department of the Army, have attempted to evaluate critically the exposure treatment of burn wounds in severe cases of second and third degree burns.

METHODS AND MATERIAL

A special "burn team" used this exposure method exclusively on ninety-four consecutive burn patients. All these burns were severe enough to require admission of the patient to the hospital. This report, however, is concerned only with an appraisal of the method as used on fifty-two of the most severe cases of second and third degree burns. These patients were all hospitalized within one to six hours following injury. As mentioned earlier, we shall not dwell at length on details of systemic therapy. It will suffice to state that initial and early treatment and supportive measures followed accepted principles. The Berkow scale was employed to estimate the extent of the body surface burned and biopsy of the doubtful areas was used to determine the actual depth of the injury.

The local treatment began in the emergency unit and proceeded simultaneously with systemic therapy. In extensive lesions, attending personnel wore cap, gloves, and mask. Gross debris was carefully removed from the wound area by lavaging with copious amounts of warm water. Then followed a gentle washing of the burn wound with pHisoHex. All vesicles were opened and loose epithelium was removed. The patient was then transferred to a stretcher and covered with sterile sheeting.

Aqueous Penicillin (600,000 units) was given on arrival at the special burn ward and then every twelve hours for seven to eight days. Further antibiotic therapy was given only for specific indications. The patient was placed in bed on sterile sheets and postured to allow for the most complete exposure of the wound areas. A tent effect was produced by placing a second sterile sheet over a bed cradle. Both ends were left open, to aid the circulation of air about the patient. The windows and doors of the burn ward were screened. During the first forty-eight to seventy-two hours of care, all attending personnel used the aseptic technique. Oral, tube, or gavage feedings

Fig. 1.—A 42-year-old man who sustained 58 per cent second and third degree burns of body surface from gasoline flames. Photographed on third day postburn.

Fig. 2.—Back view of patient in Fig. 1, photographed third day postburn.

Fig. 3.

Fig. 4.

Fig. 3.—Patient in Fig. 1 photographed thirteenth day postburn. Second degree burn crust separating. Areas of third degree injury under enzyme débridement.

Fig. 4.—Patient in Fig. 1 photographed showing thirteenth day posterior aspect. Note epithelization, also some maceration about arm and chest areas of juxtaposition.

Fig. 5.

Fig. 6.

Fig. 5.—A 3-year-old Negro female child who sustained 68 per cent second and third degree burns when clothes caught fire. Photographed on second day postburn.

Fig. 6.—Patient in Fig. 5 photographed ten days postburn. Eschar intact over second and third degree areas. Child was at ease, was encouraged to stand, and she turned frequently in bed.

were usually started within twenty-four hours. Hourly observation of urinary output was facilitated by the routine use of the indwelling catheter in burns of 20 per cent or more, or in cases where the patient was admitted in shock. Demerol Hydrochloride was our choice of analgesic. Burns of both volar and dorsal surfaces posed a serious problem and every effort was made to allow for equalization of the drying process and avoidance of maceration. Whenever possible, we started chair-sitting and early ambulation to prevent dependent surface maceration and loss of eschar. Figs. 1 to 7 illustrate the clinical aspects of treatment.

Fig. 7.—Patient in Fig. 5 photographed ten days postburn. Note eschar macerated over midportion of back. The child is afebrile at present time.

ANALYSIS

Fifty-two of the most severe second and third degree lesions will now be analyzed as shown in the succeeding tables.

Morbidity Rates.—In Table I, the severe-burn group is subdivided into 37 patients with second degree and 15 patients with third degree burns. In the

first column, it will be seen that infection presented no problem. Only 2 minor infections of 37 cases ensued. The average period of hospitalization equaled 15.6 days.

TABLE I. MORBIDITY

	SECOND DEGREE BURNS	THIRD DEGREE BURNS
Total number of patients	37	15
Total infections	2 (5%)	10 (66%)
Major	0	5
Minor	2	5
Average day postinjury infection noted	3.5	6.2
Average duration of infection	4.4	16.4
Average number of days hospitalized	15.6	45.9
Total number of patients requiring skin grafts	0	15

In the second column, a much smaller group, all patients had over 10 per cent of the body surface involved as a full-thickness burn. In many instances, additive second degree lesions were present. It is immediately apparent that infection assumes major significance in this group.

It is only fair to state at this time that our infection rate is higher than that recorded by the few other investigators working with the exposure method.[16-18]

In fact, few adequate infection rates have been noted in any of these previous reports. Possibly our own criteria for our listed minor infections have been too rigid. We have considered a persistent pyrexia of over 100° F. with no other demonstrable focus of infection elsewhere as probable evidence of subclinical infection of the burn wound, even though frank suppuration was not present.

Five patients developed a major infection, resulting in eventual death in three cases. The hospital stay averaged 45.9 days. All patients with full-thickness burns required skin grafting.

TABLE II. MORTALITY RESULTS OF SECOND DEGREE BURNS

	PER CENT OF BODY SURFACE BURNED									
	0 TO 10		10 TO 20		20 TO 30		30 TO 40		40 TO 50	
AGE (YEARS)	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY
1 to 10	4	0	1	0	–	–	–	–	–	–
10 to 20	3	0	2	0	1	0	–	–	–	–
20 to 30	1	0	3	0	0	0	–	–	–	–
30 to 40	1	0	3	0	2	0	–	–	–	–
40 to 50	2	0	3	0	0	0	–	–	–	–
50 to 60	2	0	1	0	0	0	1	0	–	–
60 to 70	0	0	5	0	1	0	0	0	–	–
70 to 80	0	0	1	0	0	0	0	0	–	–
Total	13	0	19	0	4	0	1	0	–	–
Total number of patients in group								37		
Mortality								0		

TABLE III. MORTALITY RESULTS OF THIRD DEGREE BURNS

AGE (YEARS)	PER CENT OF BODY SURFACE BURNED													
	0 TO 10		10 TO 20		20 TO 30		30 TO 40		40 TO 50		50 TO 60		60 TO 70	
	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY	NO. OF PATIENTS	MORTALITY
1 to 10	–	–	–	–	–	–	–	–	1	0	–	–	1	1
10 to 20	–	–	–	–	–	–	–	–	–	–	–	–	–	–
20 to 30	–	–	–	–	–	–	1	0	–	–	–	–	–	–
30 to 40	–	–	1	0	1	0	1	0	–	–	–	–	–	–
40 to 50	–	–	2	0	2	0	–	–	1	0	–	–	–	–
50 to 60	–	–	–	–	–	–	–	–	–	–	–	–	2	2
60 to 70	–	–	–	–	–	–	–	–	–	–	1	1	–	–
70 to 80	–	–	1	0	–	–	–	–	–	–	–	–	–	–
Total	–	–	4	0	3	0	2	0	2	0	1	1	3	3

Total number of patients in group 15
Mortality 4, 26 per cent

Mortality Rates.—

Second Degree Burns: In Table II the patients are grouped according to age and extent of body area burned. Although no deaths occurred in this group of second degree burns, the number of extensive surface lesions is limited. The 13 patients listed in the first column represent those with burns of the face and scalp.

Third Degree Burns: A comparison of the third degree burns (Table III) reveals the expected mortality (26 per cent), conforming with universal experience—to wit: mortality in burns is directly related to the extent of the body surface burned and advancing years. There were a total of 4 fatalities with patients either having burns in excess of 50 per cent or being over the fifth decade of life.

Combined Results: A more specific analysis of the fatalities reveals a combined mortality of 7.6 per cent, that is, 4 deaths in 52 cases (Table IV).

TABLE IV. MORTALITY RESULTS OF COMBINED GROUP

Number of patients treated	52
Mortality	7.6 per cent
Causes of death	
Sepsis	3
Water intoxication	1
Day of death after thermal injury	42
	72
	33
	5

One of these fatalities, caused by water intoxication, occurred in a 62-year-old man who incurred a 52 per cent third degree burn. His death occurred on the fifth day after burning. The remaining 3 fatal deaths occurred in the patients' hospital course at 42, 72, and 33 days, respectively. All these were proved cases of bacteremia and this diagnosis was confirmed at necropsy.

Combined Rates: One of the most important considerations of this study is a comparison of mortality figures obtained when both methods of therapy are compared. Table V is presented with the realization that numerous other facets enter into a study of mortality rates. However, this representation

TABLE V. MORTALITY RATES IN SECOND AND THIRD DEGREE BURNS OF OVER TEN PER CENT OF THE BODY SURFACE

AUTHOR	YEAR REPORTED	NO. OF PATIENTS	MORTALITY	
			NUMBER	PER CENT
		Occlusive		
Allen and Koch*	1942	185	5	2.7
Bull and Squire	1949	339	58	17.0
Blocker and others	1951	47	4	8.5
Total		571	67	11.0
		Exposure		
Pulaski and others	1951	24	4	16.0
Blocker and others	1951	42	5	12.0
Artz and others	1952	45	7	15.4
Rousselot and others	1952	39	4	10.2
Total		150	20	13.3

*Includes first, second, and third degree burns.

indicates that the exposure method does not increase the expected mortality. In this table the numerical representations are small but salient, in that, to the best of our ability, they represent severe burns.[1, 6, 14]

An inspection of the very recent reports of Pulaski,[18] Blocker,[14] Artz,[15] and those of our own revealed striking consistency in the exposure group.

SUMMARY

The exposure method of burn therapy is a distinctly simpler procedure than the currently practiced closed form of treatment. This is attested to by the marked diminution in supplies and personnel needed to manage this regimen.

Photographs were shown illustrating the typical crust and eschar forming in effect a protective coating for these burn wounds.

The cases presented are limited to burn wounds, uncomplicated by other forms of trauma.

There is a marked diminution in hospital stay of patients treated by this method, for in third degree burns the duration of care averaged 45.9 days.

The morbidity and mortality rates in the exposure form of therapy compare favorably with the rates in the use of occlusive dressings.

The exposure treatment of burn wounds, as outlined, is a possible solution to the management of mass burn casualties.

REFERENCES

1. Allen, H. S., and Koch, S. L.: The Treatment of Patients With Severe Burns, Surg., Gynec. & Obst. **74**: 914, 1942.
2. Siler, V. E., and Reid, M. R.: Koch Method of Burn Treatment, Ann. Surg. **115**: 1106, 1942.
3. Cope, O.: The Treatment of Surface Burns, Ann. Surg. **117**: 885, 1943.
4. Evans, E. I.: The Early Management of the Severely Burned Patient, Surg., Gynec. & Obst. **94**: 273, 1952.
5. Colebrook, L. A.: A New Approach to the Treatment of Burns and Scalds, London, 1950, Fine Techn. Publ.
6. Bull, J. P., and Squire, J. R.: A Study of Mortality in a Burns Unit, Ann. Surg. **130**: 160, 1949.
7. Pearse, H. E., and Payne, T. J.: Mechanical and Thermal Injury From the Atomic Bomb, New England J. Med. **241**: 671, 1949.
8. Copeland, W. P.: The Treatment of Burns, M. Rec. **31**: 518, 1887.
9. Sneve, H.: The Treatment of Burns and Skin Grafting, J. A. M. A. **45**: 1, 1905.
10. Haas, S. V.: The Treatment of Burns in Children by Exposure to Air, Am. J. Surg. **29**: 61, 1915.
11. Wallace, A. B.: Burns: Some Experience of Local Care, Brit. J. Plast. Surg. 4: 224, 1951.
12. Pulaski, E. J., and others: Exposure (Open) Treatment of Burns, U. S. Armed Forces M. J. **2**: 769, 1951.
13. Pulaski, E. J., and others: Evaluation of the Exposure Method in the Treatment of Burns: Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, 1951, Philadelphia, 1952, W. B. Saunders Company, p. 518.
14. Blocker, T. G., and others: An Approach to the Problem of Burn Sepsis With the Use of Open Air Therapy, Ann. Surg. **134**: 574, 1951.
15. Artz, C. P., and others: The Exposure Treatment of Burns, Ann. Surg. In press.
16. Blocker, T. G., and others: An Approach to the Problem of Burn Sepsis With the Use of Open Air Therapy, Ann. Surg. **134**: 574, 1951.
17. Artz, C. P., and others: The Exposure Treatment of Burns, Ann. Surg. In press.
18. Pulaski, E. J., and others: Evaluation of the Exposure Method in the Treatment of Burns: Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, 1951, Philadelphia, 1952, W. B. Saunders Company, p. 518.

THE RELATION OF THE PANCREAS TO BLOOD COAGULATION

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THERE are many factors which affect blood coagulation, and the identification of accelerating and inhibiting substances seems to occur with increasing frequency. The relationship of pancreatic function to blood coagulation is one of the less clearly defined factors.

The coexistence of venous thrombi and carcinoma has been reported by many observers.[1-8] This observation may have formed the basis for many of the early "cancer tests." Bock and Rausche[9] postulated that a state of hypercoagulability exists in patients with carcinoma. The hypercoagulability was thought to be the cause of thrombus formation in the presence of certain carcinomas. It soon became apparent, however, that carcinoma, per se, was not able to produce a consistent or characteristic change in blood coagulation. In an attempt to ascertain in what types of carcinoma there was an increase in thrombotic tendency, Sproul undertook a monumental task. She reviewed 4,258 consecutive necropsies at the Presbyterian Hospital and was able to demonstrate the increased coexistence of venous thrombi with carcinoma of the body and tail of the pancreas over all other types of carcinoma. Interestingly enough, she demonstrated that carcinoma of the head of the pancreas was associated with venous thrombi with no more than average frequency.[10] Without suitable explanation, this has come to be recognized as a clinical fact. Indeed, a diagnosis of multiple venous thrombi may herald the presence of a neoplasm of the body or tail of the pancreas.[11-14]

These facts suggest that some factor in the pancreatic secretion has a bearing on the blood-clotting mechanism. Variations in the coagulability of blood have been observed in other forms of pancreatic disease.[15] In addition to pancreatic disease, aberrations in the clotting process have been witnessed in the laboratory animal subjected to disrupted pancreatic function.[16] Hecht[17] quotes Boldyreff, who observed that dogs with pancreatic fistulas were subject to hemorrhage. This investigator was able to demonstrate a prolonged coagulation time in these dogs during periods of pancreatic hypersecretion, while decreased coagulation times were observed during periods of hyposecretion. Closure of the pancreatic fistula resulted in a return to normal coagulation time. Boldyreff interpreted this as an experimental hemophilia and suggested that absence of a pancreatic ferment was responsible for the prolongation of coagulation. Hecht reported that cases of sporadic hemophilia were associated with an increased number of pancreatic afflictions and frequent disturbances of lipase activity.

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Bechgaard, Strombeck, and Borgstrom[18-20] found a reduced concentration of plasma prothrombin in acute and chronic pancreatitis in man. These workers hypothesized that an increase in the activity of trypsin is responsible for the destruction of prothrombin. They further reported that the decrease in prothrombin was inversely related to the quantity of urine amylase.

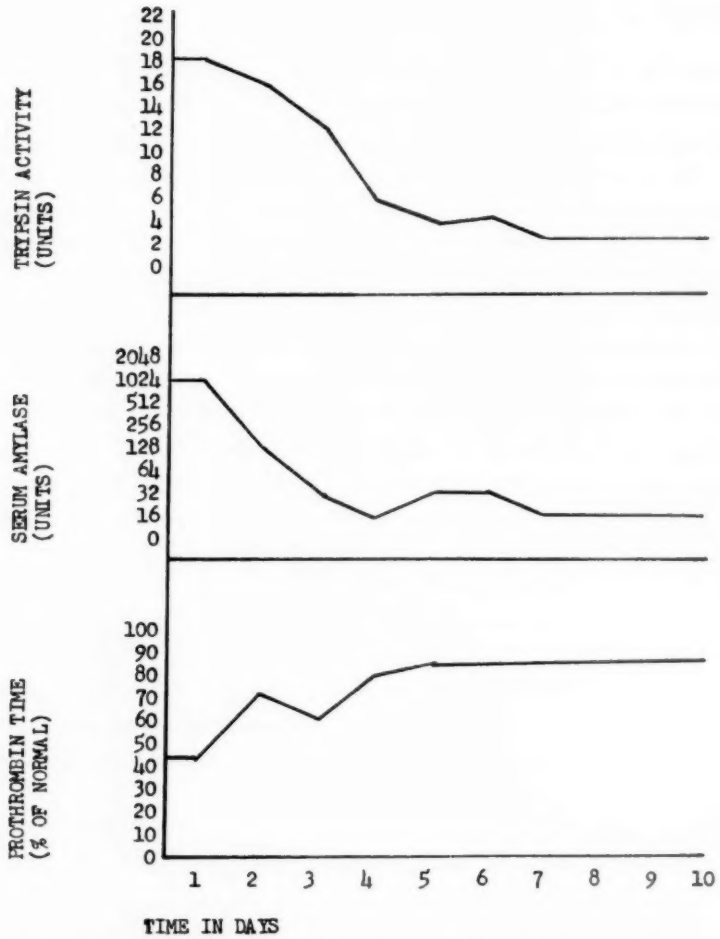

Fig. 1 (Case P. R.).—Chart showing relationship of prothrombin time, serum amylase, and trypsin activity. Quick's bedside method was used for the determination of prothrombin time. Normal range is 70 per cent to 100 per cent of normal. X-ray therapy was begun after the first day. Two hundred roentgens daily were applied to the abdomen for three days.

Lasher and associates[16] produced acute pancreatitis in dogs, attempting to correlate the changes in prothrombin concentration and coagulation times. They found a progressive lengthening of the prothrombin time and coincident prolongation of the coagulation time. They also reported similar observations in acute pancreatitis in man. We have correlated the prothrombin time and serum amylase and trypsin activity in two cases (see Figs. 1 and 2). Although these do not represent a statistically significant number of cases, the inverse relation of serum amylase and trypsin activity to prothrombin time is worthy of further consideration.

A real advance in the correlation of blood coagulation and pancreatic function has been made by Innerfield and associates.[21] These investigators have studied the plasma antithrombin patterns in disturbances of the pancreas. They offer impressive evidence that a parallel exists between plasma antithrombin and blood trypsin levels. Those diseases, that is, acute pancreatitis and chronic recurrent pancreatitis, associated with high trypsin levels show

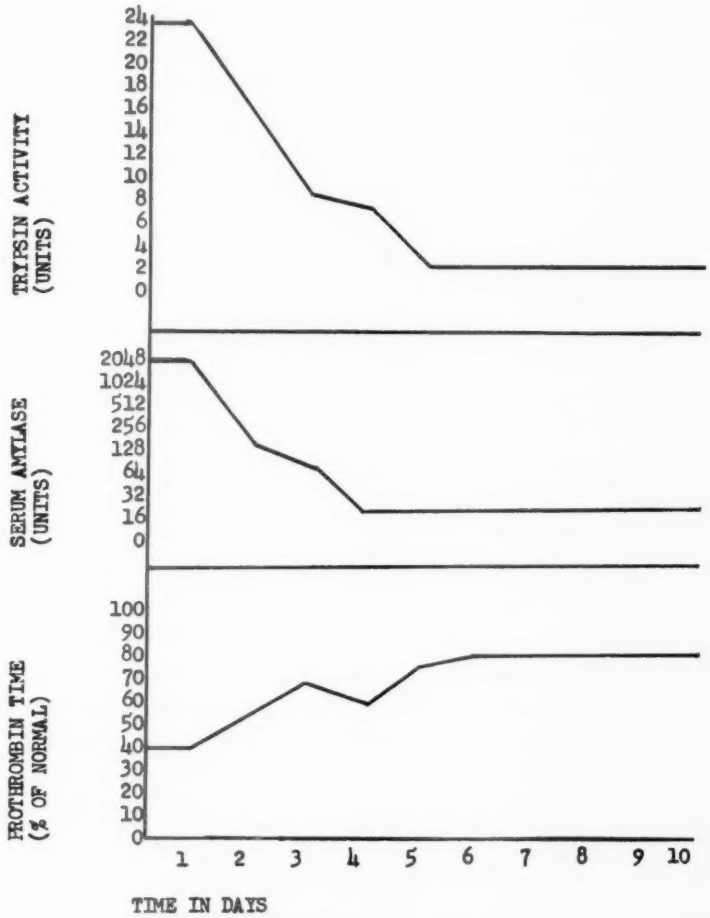

Fig. 2 (Case R. N.).—Chart showing relationship of prothrombin time, serum amylase, and trypsin activity. Quick's bedside method was used for the determination of prothrombin time. Normal range is 70 per cent to 100 per cent of normal. X-ray therapy was begun after the first day. Two hundred roentgens daily were applied to the abdomen for three days.

a corresponding increase in the quantity of plasma antithrombin. The reverse is true when the blood trypsin level is lowered. Innerfield and associates also observed the reaction of certain substances following the intravenous injection of trypsin in dogs. They noted a depression of AC globulin, prothrombin, antithrombin, and fibrinogen. This reaction is temporary for all but the antithrombin factor, which, after a brief depression, shows a sustained elevation in titer.

Rich and Duff[22] have described hyaline degeneration and necrosis of the medial coats of small arteries of the pancreas and other areas as a feature of

acute pancreatitis. Rupture of these small vessels is undoubtedly responsible for many of the frank hemorrhagic characteristics of this disease. Activated trypsin is thought to be the substance responsible for these changes. The arterial pathology has not, however, been a constant manifestation of acute pancreatitis.

From the foregoing it is evident that a relationship exists between pancreatic secretion and blood coagulation. Further clarification of this problem necessitates a review of some of the substances related to pancreatic function.

Trypsin.—Trypsin and chymotrypsin form the major portion of the proteolytic activity of the pancreatic secretion. Trypsin is responsible for carrying the digestion of protein beyond the peptose stage.[23] The ability of trypsin to coagulate blood has long been known. Acceleration of blood coagulation by trypsin was demonstrated in 1916 by Douglas and Colebrook.[24] One year later, Heard[25] reported the ability of trypsin to coagulate oxalated blood and postulated that this phenomenon is caused by a disturbance in the calcium and phosphorus content of fibrinogen. Waldschmidt-Leitz and associates[26] reported confirmatory observations on the acceleration of blood coagulation by trypsin. They theorized that trypsin and thrombin are proteolytic enzymes either identical or closely related. It was their belief that these substances hasten an enzymatic hydrolysis of fibrinogen to fibrin. It remained for Eagle and Harris[27] to elucidate the action of trypsin on the blood coagulation mechanism. These workers found that trypsin is capable of activating prothrombin to thrombin. It is uncertain whether or not trypsin actually combines with prothrombin or if prothrombin is hydrolyzed. A general conclusion may be drawn, however, that trypsin has the same effect on prothrombin as the physiologic system calcium plus platelet factor. Howell and Fuchs[28, 29] have shown that trypsin is capable of prothrombin conversion in the absence of calcium, verifying it as a true substitute for the calcium-platelet system. This ability of trypsin has been exploited in experimental treatment of hemophilia in an effort to decrease the coagulation time in that disease.[30]

Trypsin, when present in sufficient concentration, is also capable of destroying formed thrombin.[27] That the level of trypsin in the circulating blood can be maintained in sufficiently high concentration to digest clots seems doubtful.

Other proteolytic enzymes occurring in human plasma have been demonstrated. Studies have failed, however, to prove a relationship between these enzymes and physiologic blood coagulation.[31, 32] It has been established, however, that these factors are capable of accelerating platelet-deficient plasma of normal individuals. Proteolytic enzyme-inhibiting agents have been demonstrated in serum. The crude albumin fraction obtained from serum has been associated with its inhibitory action on trypsin.

The absorption of trypsin is thought to be responsible for much of the serious symptomatology of acute pancreatitis.[33-36] We have obtained trypsin levels in two cases with confirmatory evidence of acute pancreatitis, as shown in Figs. 1 and 2. In these two proved cases of pancreatitis, with initial serum amylase levels of 1,240 units and 1,024 units, respectively, trypsin activity

could be detected in peripheral venous blood. Elevations of 24 units and 18 units were found at the peak of serum amylase values. Trypsin activity rapidly declined following x-ray therapy for the pancreatitis. Some trypsin activity remained, however, after as many as four consecutive days of normal serum amylase levels. It is curious that trypsin, which is largely responsible for the morbidity which occurs with acute pancreatitis, has been almost completely ignored in the laboratory diagnosis of this disease.

We have used the method of Anson and Mirsky[37] in determining trypsin levels. It has not been found by us to be a sufficiently difficult test to preclude its routine use as an aid in the diagnosis of acute pancreatitis.

Lipase.—Sproul has studied the effects of pancreatic achylia on the blood-clotting mechanism. She has suggested that a diminution in prothrombin formation follows a decrease in the production of pancreatic lipase.[38] Vitamin K is dependent upon suitable fat digestion for its absorption in the intestine and utilization by the liver in the formation of prothrombin.[39] With diminished pancreatic secretion, it has been suggested that this chain of events may be interrupted with resultant bleeding tendency. A clinical hemorrhagic tendency following diseases associated with hyposecretion of the pancreas has not been noted, to our knowledge. Conversely, a thrombotic tendency has been the rule.

Calcium.—Calcium is never a factor in hemorrhagic disease.[40] Stefanini[41] has demonstrated that adequate coagulation occurs with levels of serum calcium of 4.6 mg. per cent.

DISCUSSION

There are varied responses to pancreatic disease in man. Among the more serious reactions are those related to alterations in blood coagulation. The frank, generalized hemorrhagic features of acute pancreatitis constitute a threat to the life of the patient. Likewise, the development of multiple venous thrombi, as a direct result of pancreatic disease, may produce phenomena of catastrophic proportions.

The relation of pancreatic enzymes to the process of bleeding and coagulation has been discussed. Evidence is offered to show that such a relationship does exist. Trypsin is apparently the most vital of the pancreatic enzymes in production of altered blood coagulability.

The immediate action of intravenous injection of trypsin is associated with a temporary decrease in plasma antithrombin. It seems logical to assume that with an increased production of trypsin, such as is seen in acute pancreatitis, a more liberal absorption of trypsin would occur in the portal system. The ability of trypsin, per se, to coagulate blood, plus the temporary diminution in plasma antithrombin titer, might lead to thrombosis of the portal system. The secondary sustained elevation of the antithrombin factor which occurs after an increase in trypsin levels may lead to peripheral hemorrhagic tendencies. We have observed a case in which these paradoxical findings were exhibited.[42]

The general vascular response to acute pancreatitis is a hemorrhagic tendency. The arterial changes described by Rich and Duff and the prolonged elevation of plasma antithrombin seem to be reason enough for such a reaction. In carcinoma of the body or tail of the pancreas, a decrease in trypsin secretion with resultant diminution of plasma antithrombin may be responsible for the occurrence of multiple venous thrombi. Carcinoma of the head of the pancreas, however, is not associated with thrombi with more than average frequency. In this type of carcinoma, the pancreatic secretion may be entirely prevented from reaching the duodenum. It would seem that this type of lesion might be more productive of thrombi than those in which the pancreatic secretion is merely diminished, that is, in carcinoma of the body and tail of the pancreas, if credence is given to the theory that decreased pancreatic secretion of trypsin is the cause of thrombi with carcinoma of the body or tail. It may be that in carcinoma of the head of the pancreas, a thrombotic tendency is offset by the disturbance of prothrombin function secondary to occlusion of the common duct.

CONCLUSIONS

1. Multiple venous thrombi are more frequently associated with carcinoma of the body or tail of the pancreas than with other types of carcinoma.

2. A hemorrhagic tendency is a characteristic finding in acute pancreatitis.

3. Alterations in trypsin levels are responsible for certain modifications of blood coagulation.

4. Two cases are presented in which the relation of prothrombin times and serum amylase and trypsin levels are correlated.

REFERENCES

1. Umlauft, W.: Thrombosen und Pankreaskarzinom, München. med. Wchnschr. **80**: 607-608, 1933.
2. Thoenes, E.: Multiple Venenthrombosen ein bisher unbekanntes Frühsymptom bei Pankreaskarzinomen, München. med. Wchnschr. **79**: 1677-1678, 1932.
3. Winter, R.: Ueber die Entstehung von Thromben im rechten Herzen und in den Aesten der Lungenschlagader, Virchows Arch. f. path. Anat. **282**: 99-106, 1931.
4. Smith, R. E.: Case of Latent Carcinoma Causing Migratory Multiple Venous Thrombosis, Guy's Hosp. Rep. **82**: 437-439, 1932.
5. McFarland, J.: A Case of Carcinoma of the Pancreas, Proc. Path. Soc. Philadelphia **2**: 112-114, 1899.
6. Gray, S. H.: Spontaneous Rupture of the Spleen Following Venous Thrombosis in Carcinoma of the Pancreas, Arch. Path. **6**: 433-435, 1928.
7. Thompson, A. P.: Thrombosis of the Peripheral Veins in Visceral Cancer, Clin. J. **47**: 137-140, 1938.
8. Ferris, E. B., and Ritterhoff, R. J.: Multiple Venous Thromboses With Associated Carcinoma of the Pancreas, Ohio State M. J. **41**: 437-440, 1945.
9. Bock, H., and Rausche, C.: Significance of Blood Coagulation Valency in Carcinoma Diagnosis, Zentralbl. f. Chir. **53**: 1440-1441, 1926.
10. Sproul, E. E.: Carcinoma and Venous Thrombosis: The Frequency of Association of Carcinoma in the Body and Tail of the Pancreas With Multiple Venous Thrombosis, Am. J. Cancer **34**: 566-585, 1938.
11. Kenney, W. E.: Association of Carcinoma of the Body and Tail of the Pancreas With Multiple Venous Thrombi, SURGERY **14**: 600-609, 1943.
12. Brown, S.: Mesenteric Venous Occlusion, South. M. J. **49**: 242-249, 1940.
13. Douglas, J.: Mesenteric Vascular Occlusion, Ann. Surg. **102**: 634-636, 1935.
14. Dempsey, W. S., and Jones, T.: Venous Mesenteric Thrombosis, Cleveland Clin. Quart. **15**: 140-142, 1948.
15. Begtrup, H.: Pancreatic Disease Combined With Vitamin-K-Refractory Hypoprothrombinemia, Acta med. Scandinav. **129**: 33-36, 1947.

16. Lasher, E. P., Jr., and McCabe, Mary Margaret: Changes in Coagulation Time Associated With Experimental Acute Pancreatitis in Dogs, Arch. Surg. **60**: 164-169, 1950.
17. Hecht, E.: Blood Clotting and the Pancreas, Acta med. Scandinav. **129**: 311-320, 1947.
18. Bechgaard, P.: Acute Pancreatitis, Ugesk. f. laeger **103**: 1523-1541, 1941.
19. Borgstrom, S.: Chronic Pancreatitis, Acta chir. Scandinav. **90**: 419-431, 1944.
20. Strombeck, J. P.: Acute Pancreatitis, Zentralbl. f. Chir. **68**: 1834-1851, 1941.
21. Innerfield, I., Angrist, A., and Benjamin, J.: Plasma Antithrombin Patterns in Disturbances of the Pancreas, Gastroenterology **19**: 843-855, 1951.
22. Rich, R., and Duff, J.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **58**: 212-259, 1936.
23. Best, C., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 4, Baltimore, 1945, Williams & Wilkins Company, p. 449.
24. Douglas, S. R., and Colebrook, L.: Trypsin in Blood Cultures, Lancet **2**: 180-181, 1916.
25. Heard, W. N.: Calcium and Phosphorus of Blood, J. Physiol. **51**: 294, 1917.
26. Waldschmidt-Leitz, E., Stadler, P., Steigerwaldt, F.: Ueber Blutgerinnung, Ztschr. f. physiol. Chem. **183**: 39-59, 1929.
27. Eagle, H., and Harris, Tzvee N.: Studies in Blood Coagulation: The Coagulation of Blood by Proteolytic Enzymes (Trypsin and Papain), J. Gen. Physiol. **20**: 543-560, 1936-37.
28. Howell, W. H.: The Nature and Action of Thromboplastic Substance of the Tissue, Am. J. Physiol. **31**: 1-21, 1912.
29. Fuchs, H. J.: Die Gewinnung stabilen Menschenplasmas ohne Zusatz gerinnungshemmender Substanzen, Arch. f. exper. Zellforsch. **14**: 334-340, 1933.
30. Tagnon, Henry J.: Effect of Intravenous Injection of Trypsin on Blood Coagulation Time in Hemophilia, Proc. Soc. Exper. Biol. & Med. **57**: 45-57, 1944.
31. Ratnoff, O. D., Hartman, R. C., and Conley, C. L.: Studies on Proteolytic Enzymes in Human Plasma, J. Exper. Med. **91**: 123-133, 1950.
32. Grob, David: Proteolytic Enzymes: Further Studies on Protein, Polypeptides and Other Inhibitors of Serum, Proteinase, Leucoproteinase, Trypsin and Papain, J. Gen. Physiol. **33**: 103-124, 1949-1950.
33. Morse, Louis, and Achs, Samuel: Acute Pancreatitis, Ann. Surg. **130**: 1044-1058, 1949.
34. Blatchford, F. W., and Christofer, F.: Acute Pancreatitis, Quart. Bull., Northwestern Univ. School **22**: 198-206, 1948.
35. Fallis, L. S.: Acute Pancreatitis, J. Internat. Coll. Surgeons **16**: 37-42, 1951.
36. Howard, J., Krehl-Smith, A., and Peters, J. J.: Acute Pancreatitis: Pathways of Enzymes Into the Blood, SURGERY **26**: 161, 1949.
37. Anson, M. L., and Mirsky, A. E.: The Estimation of Trypsin With Hemoglobin, J. Gen. Physiol. **17**: 151-157, 1933-1934.
38. Sproul, E. E., and Sanders, E. K.: The Effect of Pancreatic Achylia on Vitamin K Absorption and Prothrombin Time, Am. J. Physiol. **135**: 137-148, 1941.
39. Thompson, C., and Hilferty, D. J.: The Clinical Administration of Vitamin K, M. Clin. North America **33**: 1685-1708, 1949.
40. Best, C., and Taylor, N. B.: The Physiologic Basis of Medical Practice, ed. 4, Baltimore, 1945, Williams & Wilkins Company, p. 93.
41. Stefanini, M.: Studies on the Role of Calcium in the Coagulation of Blood, Acta med. Scandinav. **136**: 250-266, 1950.
42. Storer, J., Kazdan, P., and Bilton, J.: Mesenteric Venous Thrombosis: Suggested Etiology and Case Report, Am. J. Surg. **84**: 636-640, 1952.

SPINAL COMPLICATIONS FOLLOWING LUMBAR PUNCTURE

A Review of the Literature and Report of Four Cases

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THE first lumbar puncture was performed by Quincke[1] in 1891 as a therapeutic measure in a patient with increased intracranial pressure. Since then, this procedure has been used hundreds of thousands of times for diagnosis, therapy, and spinal anesthesia. As the number of spinal taps increased, complications such as headache, diplopia, backache, paraesthesia in the legs, paralysis or weakness of the leg muscles, and meningitis were reported.[2-5]

Injury of the intervertebral disc or vertebrae as a complication following lumbar puncture, however, was not recorded until thirty-three years after the introduction of the technique. In 1924, Billington[6] reported thirty-five cases of spondylitis following lumbar puncture. Of nineteen cases, there were definite clinical evidences of spondylitis with positive x-ray findings in fourteen. The remaining sixteen cases included psychoneurotics and malingerers without evidence of true spondylitis. An intensive search of the literature on the subject from 1924 to the present reveals thirty-four additional cases.

In most of the reported cases, the injury has not been accompanied by infection. However, there are three recorded instances of osteomyelitis of the spine following lumbar puncture.[7-9]

Four instances of osteomyelitis of the spine following lumbar puncture are reported in this communication (two from the New York Hospital and two from the Hospital for Special Surgery). (See Table II.) Including these, the total of reported cases of injury to the intervertebral disc or vertebra following spinal puncture is fifty-seven. Although this is a very small number in light of the many lumbar punctures performed, the complication is a serious one that must be kept in mind whenever the procedure is performed.

Despite the usually taught concept that a snap is felt when the needle passes the dura mater, no single criterion of passage of the needle into the subarachnoid space can be relied upon. Until there is free flow of spinal fluid the exact location of the needle point is unknown.

In 1935, Pease,[10] performing lumbar punctures on cadavers, found it impossible to determine when the point of the needle was actually in the neural canal. In some patients there was a slight decrease in resistance when the canal was reached, but this occurred only when the needle was introduced very delicately. If the needle was pushed in too far, it was impossible to tell when it struck the intervertebral disc or passed into it. On the other hand, there was no difficulty in recognizing when the needle point struck a bony portion of the vertebra. Further experimental punctures on cadavers revealed several possible terminations if the needle was pushed beyond the neural canal, the most common sites being (1) the intervertebral disc, (2) a vertebra, (3) interarticular facets, and (4) venous sinusoids in the vertebral body.

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Pease describes the intervertebral disc as being composed of superior and inferior cartilaginous plates, the annulus fibrosus, and the nucleus pulposus. The annulus fibrosus is thicker anteriorly than posteriorly. This difference, plus the close union with the anterior longitudinal ligament, makes the disc much stronger and more powerful in front. The nucleus pulposus occupies from one-half to one-sixth the volume of the intervertebral disc, varying inversely with age and becoming more firm and solid with age. The nuclear material is a translucent, semigelatinous fluid through which are interspersed fine fibrous strands. Although the nucleus pulposus appears to be well demarcated from the annulus fibrosus on superficial examination, closer examination reveals a gradual blending of the former into the latter.

In flexing the spine, the pressure within the intervertebral disc increases as the anterior portions of the bodies come in closer approximation, causing a slight bulge of the disc and its nuclear material posteriorly. Pease postulated that the needle puncturing the nuclear portion of the disc permits this fluid to escape, leading to a thinning of the intervertebral space and consequent trauma to the adjacent vertebral bodies. In addition to this purely mechanical trauma, he stated that it was possible for the needle also to carry microorganisms into the intervertebral disc or vertebrae, thus setting up a localized infectious process.

If this nuclear material is extruded through a crack or other defect in the cartilaginous plate into the spongiosa of the adjacent vertebral body, an invasive reaction is set up in the bone. The semifluid material is transformed into a cartilaginous nodule (Schmorl body) and the bone about it becomes sclerosed.[11]

Milward and Grout[12] concluded that the initial injury is caused by impingement of the needle on the annulus fibrosus. This is followed by an inflammatory reaction in the disc, leading to a gradual escape of the nucleus pulposus and subsequent changes as discussed earlier by Pease.

Thus, four mechanisms leading to the development of intervertebral disc or vertebral injury following lumbar puncture are recognized: (1) puncture of annulus fibrosus with escape of nuclear material and consequent thinning of the intervertebral disc, (2) impingement of the needle on the annulus fibrosus, setting up inflammatory reaction in the disc which leads to a gradual escape of nuclear material and subsequent thinning of the intervertebral disc, (3) extrusion of nuclear material into adjacent vertebral bodies through a crack or defect in the cartilaginous plate, leading to development of Schmorl body, sclerosis of surrounding bone, and thinning of the intervertebral disc, (4) introduction of microorganisms into the intervertebral disc or vertebrae by spinal needle.

Keyes and Compere[13] exposed the vertebral bodies in sixteen dogs, opened the intervertebral discs with a small knife, and curetted out the nuclear material. In two of these animals there was a mild infection which persisted for from two to three weeks. Subsequent x-ray examination revealed disappearance of the intervertebral disc. The adjacent bony surfaces became markedly sclerosed with spur formation and lipping of the anterior edges. They found that if the cartilaginous plate of the intervertebral disc of the dog is injured by a scalpel

or drill, the nuclear material prolapses into the spongiosa, and the cartilage nodule (Schmorl body) forms. If the nuclear material is allowed simply to escape, the rest of the disc becomes thinned out and the margins of the adjacent vertebrae become sclerosed with subsequent marginal lipping.

The signs and symptoms of spinal injury in the recorded cases are strikingly similar. Immediately following lumbar puncture, or as long as six months after, the patient complains of low-back pain with or without reference of pain down the thighs, limitation of motion of the lumbar spine, weakness of the back muscles, and difficulty in walking, stooping, and lifting. Physical examination reveals rigidity of the spine, loss of lumbar lordosis, spasm of the erector spinae muscles, and tenderness over the lumbar spines. Roentgengraphic changes consist chiefly in thinning of the involved intervertebral disc, narrowing of the space between respective vertebral arches, and interarticular facets, together with sclerosis of the vertebral bodies; rarefaction and destruction of the vertebral bodies are also seen.

TABLE I

SERIES	DATE	NUMBER OF CASES	ONSET OF SYMPTOMS (TIME SINCE LAST LUMBAR PUNCTURE)	TREATMENT
Billington[6]	1924	19 (ages not given)	Not given	Lumbar puncture for therapy
Pease[10]	1935	12 (children)	Immediate to 2 weeks	5 lumbar punctures for diagnosis 5 lumbar punctures for therapy 1 lumbar puncture for encephalogram 1 spinal anesthesia
Milward and Grout[12]	1936	5 (24 to 51 years old)	Immediate to 6 months	Spinal anesthesia
Gellman[11]	1940	1 (14 years)	Immediate	Lumbar puncture for diagnosis
Deming and Zaff[14]	1942	2 (65 to 71 years)	5 days to 2 weeks	Spinal anesthesia
Everett[15]	1942	3 (21 to 29 years)	Few days to 2 months	2 lumbar punctures for diagnosis 1 spinal anesthesia
Epps[16]	1942	1 (27 years)	2 to 3 weeks	Lumbar puncture for therapy
Stewart and Owen[17]	1943	1 (23 years)	Immediate to 10 days	Spinal anesthesia
Stump and Narins[18]	1943	1 (12 years)	5 months	Spinal puncture for therapy
Findlay and Kemp[7]	1943	1 (1 month)	4 days	Lumbar puncture for diagnosis
Martin[19]	1946	1 (32 years)	2 months	Lumbar puncture for diagnosis
Baker[20]	1946	1 (4 years)	Few days	Lumbar puncture for diagnosis
James[8]	1946	1 (4.5 years)	1 week	Lumbar puncture for diagnosis
Brown and Hoffman[21]	1948	2 (26 to 29 years)	2 to 4 months	After paravertebral block
Goldenberg and Brooks[22]	1949	1 (37 years)	32 days	Lumbar puncture for diagnosis
Bromley, Craig, and Kessel[9]	1949	1 (12 years)	Not given	Lumbar puncture—reason not known
Total		53	Immediate to 6 months	

In a case reported by Findlay and Kemp[7] x-ray changes were apparent eighteen days following lumbar puncture. In the general literature, radiographic evidence of intervertebral disc or vertebral injury is recorded as occurring as early as a few weeks to as long as six months following lumbar puncture.

The reported cases from 1924 to 1951 are summarized in Table I.

Fig. 1 (Case 1).—Roentgenogram of lumbosacral spine (Nov. 23, 1948) showing diminished lordosis and lumbosacral angle. No productive or destructive changes are noted in the bones or joints.

CASE REPORTS

CASE 1 (Hospital for Special Surgery H54-444).—M. A., a 33-year-old white man, was admitted on Dec. 13, 1948, with a chief complaint of low-back pain. He had had chronic recurrence of the low-back pain for the past nine years following a lifting injury. About five weeks prior to admission he noted radiation of the pain into the left leg and both buttocks. The pain was intensified by coughing and sneezing. The past history and system review were unremarkable. Family history revealed that his mother had arthritis of the arms and back.

Physical examination revealed flattening of the lumbar lordotic curve, limitation of motion of the lumbar spine in all planes, and a dorsolumbar scoliosis to the left. There was paraspinous muscle spasm, greater on the right. Straight leg raising was limited to 35 degrees on the right and 20 degrees on the left. Knee jerks were present bilaterally but were greater on the right. Ankle jerk was absent on the right, active on the left. There were no sensory changes. The remainder of the physical examination was unremarkable. Urinalysis and hemogram were within normal limits except for a white blood count of 12,000. Sedi-

mentation rate was 25 mm. per hour. Roentgenograms of the lumbar spine taken in the clinic prior to admission (Nov. 23, 1948) revealed diminished lordosis and lumbosacral angle (see Fig. 1). No productive or destructive changes were noted in the bones or joints.

On the day after admission (Dec. 14, 1948), Pantopaque myelography was performed. The spinal needle was introduced at the level of L_2 to L_3 with great difficulty and had to be repeated many times before a free flow of spinal fluid was obtained. The myelogram revealed changes consistent with herniated disc at L_4 to L_5. At operation on Dec. 17, 1948, a herniated intervertebral disc at L_4 to L_5 and a degenerated disc at L_5 to S_1 on the left were excised without difficulty. Postoperatively the course was benign. On Jan. 11, 1949, the patient was discharged and was placed on back, leg, and abdominal exercises.

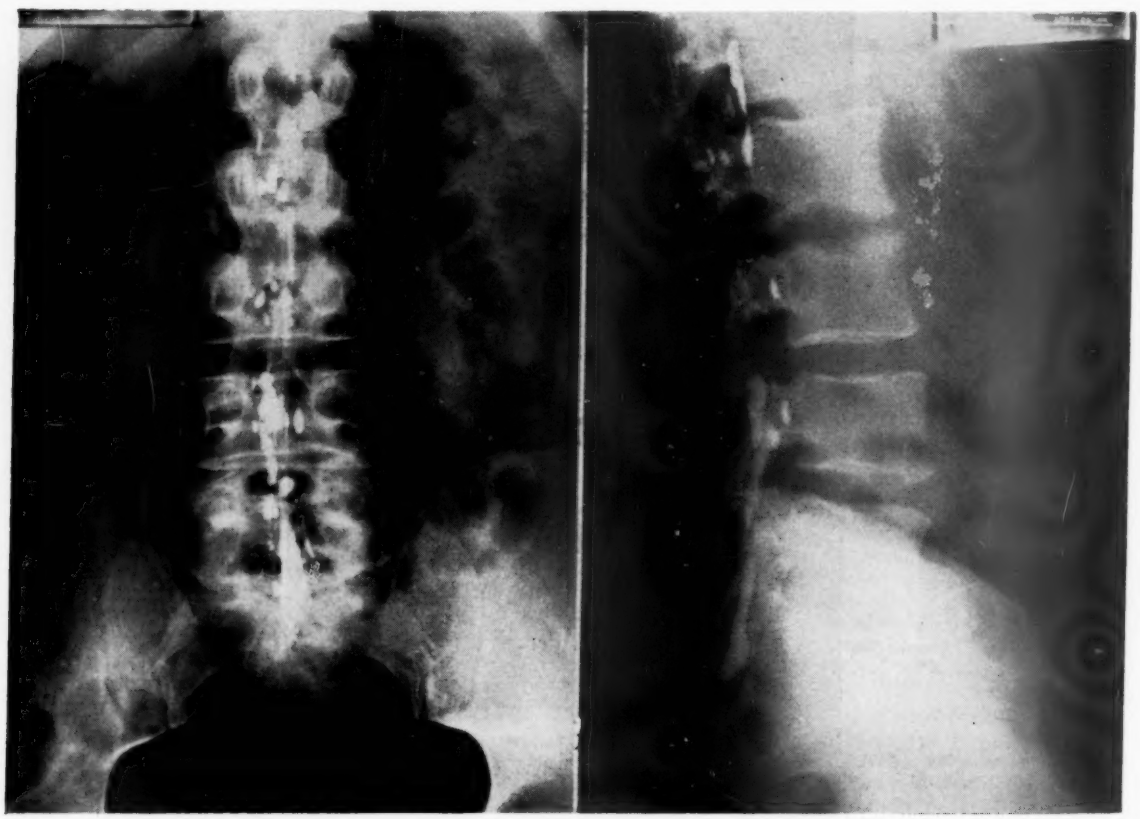

Fig. 2 (Case 1).—Roentgenograms of lumbosacral spine (Feb. 21, 1949) nine weeks after lumbar puncture. There is absent lumbar lordosis and considerable thinning of the disc between L_2 and L_3 with irregular erosions on the adjacent bony surfaces. These findings are consistent with osteomyelitis involving L_2 and L_3.

During the first week of February he was seen in the clinic complaining of considerable difficulty in the back of about one week's duration. It was noted at that time that his posture was peculiar and that he walked and stood with hyperextension of the lumbar spine and forward flexion of the dorsal spine. He had muscle spasm in both flanks and was unable to bend forward without excruciating pain. At home on complete bed rest with bed boards he felt well until one day prior to admission (Feb. 10, 1949), at which time he developed such severe pain in his back that the attention of a local physician was required and morphine had to be administered.

On Feb. 11, 1949, he was admitted for the second time with complaints of back and flank pain and muscle spasm at about the level of L_1 to L_2. There was no radiation of the pain down the legs. Physical examination revealed straight leg raising to 135 degrees

bilaterally. Passive lumbar flexion was limited 50 per cent by lumbar tightness. There was tenderness over the left paravertebral muscles opposite L_3 but nowhere else. Urinalysis and hemogram were within normal limits. Sedimentation rate was 83 mm. per hour. The patient was placed on bed boards at bed rest for three weeks without improvement. On Feb. 21, 1949 (approximately nine weeks after the lumbar puncture) roentgenograms of the lumbosacral spine revealed absent lumbar lordosis. There was considerable thinning of the disc between L_2 and L_3 and irregular erosions were seen on the adjacent bony surfaces. These changes were interpreted as indicative of osteomyelitis involving L_2 to L_3. There was no evidence of paraspinal abscess or destructive changes in any other bones. Retained Pantopaque was noted scattered through the lumbar canal and the lumbocaudal sac (see Fig. 2). The patient continued on bed rest and was placed on large doses of penicillin and sulfadiazine. Later streptomycin was administered. After about one month of this treatment the paravertebral tenderness disappeared and the patient felt more comfortable.

Fig. 3 (Case 1).—Roentgenograms of lumbosacral spine (March 20, 1950) revealing solid bony bridging between L_2 and L_3 and mature healing of the original lesion without evidence of activity.

On March 28, 1949, roentgenograms of the lumbosacral spine showed slight further destruction of the bone on the superior surface of L_3 so that the intervertebral space above looked considerably wider than average. Considerable lime deposit was found bridging L_2 to L_3 laterally. Sedimentation rate on April 13, 1949, was 48 mm. per hour and the patient was well enough to be allowed up, bearing weight with his brace. Roentgenograms on April 18, 1949, revealed increase in the lime deposit bridging L_2 to L_3 laterally and no further increase in the extent of the destruction of the adjacent surfaces of L_2 to L_3. Sedimentation rate on April 25, 1949, had fallen to 33 mm. per hour and a walking body plaster jacket was applied. The patient did well in his plaster cast and on May 3, 1949, was discharged,

much improved, to be followed in the clinic. Roentgenograms of the lumbosacral spine on May 31, 1949, revealed extensive repair about L_2 to L_3, and it was noted that the bony bridging laterally between the bodies seemed to afford perfect splinting. The plaster cast was removed and a back brace applied. The patient continued to do well and on Sept. 20, 1949, he was referred to Physiotherapy for instructions in back-strengthening exercises and was advised to go without the brace except during periods of activity. By the end of December, 1949, he was no longer wearing his brace and was completely asymptomatic. Sedimentation rate had fallen to 19 mm. per hour.

The roentgenograms of the lumbosacral spine taken Dec. 7, 1949, showed the lesion of the disc and the adjacent surfaces of L_2 to L_3 to look maturely healed. The last roentgenograms on March 20, 1950, revealed mature healing of the lesion without any evidence of activity. Solid bony bridging was present between L_3 and L_2 (see Fig. 3). Scattered drops of Pantopaque was still visible (as they had been on all the previous films) throughout the lower neural canal. The patient has remained asymptomatic since.

CASE 2 (Hospital for Special Surgery H57-155).—G. K., a 67-year-old white man, was admitted to this hospital for the first time on Feb. 21, 1950, with a complaint of frequency of one and one-half years' duration. At that time he had a transurethral resection of the prostate under spinal anesthesia (L_4 to L_5 entered without difficulty). Pathologic examination of the specimen revealed adenocarcinoma of the prostate. Following discharge, the patient did well on hormone therapy for about fifteen months. He then developed frequency again and was admitted for the second time on May 29, 1951. Roentgenograms of the lumbosacral spine on admission revealed thinning of the disc in the lumbosacral joint and between L_4 to L_5 with sclerosis and lipping of the adjacent bony surfaces, and with considerable osteoarthritic changes in their posterior articulations. On May 31, 1951, a second transurethral resection of the prostate was performed under spinal anesthesia. Lumbar puncture at this time was performed with a great deal of difficulty. Three spaces were attempted, and the fluid was finally obtained at the level of L_4 to L_5. Postoperatively the patient did well, and was discharged on June 6, 1951. Shortly after discharge he developed a urethral spasm which required a third admission. This condition was treated without difficulty.

On Aug. 6, 1951, he was admitted for the fourth time, complaining of sharp suprapubic and perineal pain after micturition. Shortly after admission a suprapubic cystotomy was performed as well as a bilateral vasectomy and biopsy of the bladder wall. On Aug. 22, 1951, the patient was discharged generally improved.

He was admitted for the fifth time on Oct. 30, 1951, with abdominal and pelvic pain. He complained also of low-back pain with some reference of pain down the legs. Roentgenograms of the lumbosacral spine on the day of admission (five months after lumbar puncture) revealed considerable thinning of the disc between L_4 and L_5 as compared with previous films of May 29, 1951. There was a moth-eaten irregularity of the adjacent vertebral bodies. The findings suggested a low-grade infectious process involving the disc and adjacent bony surfaces as the result of the difficult spinal puncture previously performed. Nothing was seen in any of the bones to indicate the presence of metastasis. On physical examination, the patient was observed to have a stony hard prostate that appeared to invade the rectum on either side. The patient was subjected to bilateral orchiectomy on Oct. 31, 1951. Following this he was placed on bed boards at bed rest and was given antibiotic therapy. The back pain subsided slightly and he was discharged on Nov. 6, 1951, with a back brace. It was planned to follow the patient with frequent lumbosacral spine roentgenograms to observe the progress of the osteomyelitic process at L_4 to L_5. However, about one month after discharge, the patient died at home. A post-mortem examination was not performed.

CASE 3 (New York Hospital 345702).—M. G., a 2-month-old white male infant, was admitted on Dec. 3, 1942, because of a birth injury. On the second day of life he became cyanotic and hypertonic with twitchings. At that time he was admitted to another hospital

where he received a blood transfusion and had a lumbar puncture performed. The mother was told that the child had an intracranial hemorrhage. Since then he had been hypertonic and spastic with many episodes of twitching and hyperexcitability.

On admission he was a very jumpy and nervous baby, continually twitching, who seemed to be in pain. His temperature was 39° C. The arms and legs twitched. The child had a high-pitched shrill cry. There was a diffuse firm mass over the lower lumbar region, measuring 4 by 5 cm., covered with apparently normal skin and dark hair. The spine was angulated posteriorly, and for 2 cm. below this angulation no spinous processes or sacral vertebrae could be felt. The right foot was held slightly everted.

Urinalysis was within normal limits. Hemogram revealed hemoglobin of 10 Gm., white blood count 30,000. During his hospital stay the hemoglobin fell as low as 8.3 Gm. and, following transfusions, rose to as high as 11.7 Gm. The white blood cell count varied between 10,000 and 21,000. The spinal fluid, on his admission, contained sugar 45 mg. per cent, chlorides 624 mg. per cent, protein 50 mg. per cent. Culture of the spinal fluid was negative; no cells were noted.

Roentgenograms of the spine on Dec. 3, 1942 (about two months after the lumbar puncture), revealed that the adjacent portions of the bodies of L_3 and L_4 were involved in a destructive process with partial collapse of each body and involvement of the intervertebral disc space. Incomplete fusion of the neural arches of the lower lumbar vertebrae was noted. There was a moderate soft tissue swelling present over the lower lumbar region. These changes were felt to be consistent with osteomyelitis of L_3 to L_4.

During the first week in the hospital the infant gained weight and remained afebrile. He received several blood transfusions and was placed on sulfadiazine. A repeat roentgenogram of the lumbosacral spine on Dec. 16, 1942, showed progression of the destructive process in L_3 and L_4. At the region of the psoas on the right there was some evidence of a soft tissue mass. Beginning with the second week after admission, the infant's course was steadily downhill with daily fever as high as 40° C. His general condition was extremely poor and the patient died on Dec. 24, 1942. Permission for autopsy was not obtained. Post-mortem spinal fluid was unremarkable. Post-mortem blood culture grew out five to six colonies of *Staphylococcus aureus hemolyticus.*

Case 4 (New York Hospital 330364).—J. J., a 61-year-old white man, was admitted on June 5, 1942, with a two-year history of progressive slowing of the urinary stream. Except for an enlarged, soft, and boggy prostate, the physical examination was unremarkable. Routine laboratory work was within normal limits. During this admission, external urethrotomy and a perineal prostatectomy for benign prostatic hypertrophy were performed under spinal anesthesia given at the level of L_4 to L_5. Thirty-six hours postoperatively the patient developed a small pulmonary embolus from which he recovered without incident. About ten days following his prostatectomy, the perineal wound began to drain urinary and fecal material. Rectal examination revealed a defect just within the anus on the anterior wall of the rectum. Bladder urine was noted to contain fecal matter. Under local treatment the drainage decreased, and on July 7, 1942, the patient was discharged generally improved.

A few months following discharge he had an unsuccessful repair of the vesicorectal fistula at another hospital. Shortly after this he developed an abscess in the left abdomen which was treated elsewhere. He was admitted again on April 17, 1943, for correction of the draining sinus on the left abdomen and unresponsive vesicorectal fistula. Except for these defects, physical examination was unremarkable. Laboratory work was within normal limits. Two days following admission (April 19, 1943) a suprapubic cystotomy was performed under spinal anesthesia (L_3 to L_4). At the same time the left abdominal sinus was explored but its entire extent could not be determined.

Postoperatively the course was poor. There was a pussy discharge from the suprapubic wound, and urine and feces continued to pass through the rectovesical fistula. Accordingly, the fecal stream was diverted by a colostomy on May 3, 1943, performed under spinal anesthesia (level not indicated). This was revised on June 3, 1943, under local anesthesia. About the middle of June, 1943 (two months postcystotomy), the patient developed an

abscess over the lumbar area of the back. This was opened and pus was drained. Roentgenograms of the lumbosacral spine taken on June 18, 1943, revealed destruction of the intervertebral cartilage between L_3 and L_4 with irregularity of the joint margins and narrowing of the intervertebral space. Evidence of bony sclerosis of the bodies of L_3 and L_4 was also noted. Repeat roentgenograms on July 26, 1943, again demonstrated the osteolytic process involving L_3 and L_4, with considerable destruction of the intervertebral disc at that point. The films indicated no increase or decrease in the process since the previous examination.

On Aug. 18, 1943, the patient developed swelling, redness, and tenderness over the right lower leg. Roentgenograms of this extremity revealed a cortical abscess of the right tibia interpreted as a metastatic focus of the osteomyelitis of the spine. He was placed on penicillin with little improvement in the condition, and in the ensuing two to three months developed many abscesses over his back which were incised and drained without success.

Roentgenograms of the spine taken at frequent intervals from July to December, 1943, showed slight filling-in of the bony defect in the anterior superior margin of L_4 with no evidence of increased destruction. The intervertebral space between L_3 and L_4 was almost completely absent.

Films taken on Jan. 31, 1944, revealed almost complete sclerosis and obliteration of the posterior two-thirds of the intervertebral joint space between L_3 and L_4. There was a filling-in of the bony trabecular structure in the anterior portion of the vertebral bodies with excessive osteophytic formation bridging the anterior left lateral surfaces. These findings were further evidence of healing. There was no detectable change at this time in the osteomyelitic process in the tibia. On Feb. 25, 1944, the patient was discharged, still contending with recurrent abscesses of the back from the old osteomyelitis of L_3 to L_4 and metastatic osteomyelitis of the right tibia.

Following discharge he was well until May of 1944, at which time he developed an abscess in the left groin which ruptured and drained for several days. Two days later he developed fever and pain in the low back and was admitted for the third time on Sept. 29, 1944, with a draining sinus in the left lower quadrant. Roentgenograms on admission revealed no evidence of activity of the osteomyelitis of the right tibia. Spinal films showed further obliteration of the joint space between L_3 and L_4 and greater bridging along the left side of the vertebral bodies with persistent loss of normal bone trabecular structure in the anterior portion of L_4. No evidence of activation of the osteomyelitis was present in the lumbar spine. The patient was placed on penicillin. Drainage from the sinus decreased, and there was evidence of healing at the time of his discharge on July 11, 1944.

However, he subsequently developed a psoas abscess on the right, and had a fourth admission for incision and drainage of this abscess on Aug. 28, 1944. Postoperatively he did well, and he was discharged on Oct. 25, 1944, greatly improved. Roentgenograms at the time of discharge revealed no evidence of activity of the old osteomyelitis at L_3 to L_4.

The patient had four more admissions during 1945 and 1946 because of recurrent right psoas abscess, perirectal abscess, abscess of the right flank and groin, and abscess of the back. These were treated by incision and drainages with variable success.

On March 8, 1947, the patient was admitted for the ninth time for acute epididymitis. Re-examination of the lumbosacral spine at this time again revealed almost complete obliteration of the intervertebral joint space between L_3 and L_4 and extensive bony bridging between several of the lumbar segments, particularly on the left side. Mottled coarsening of the bone trabecular structure was once more seen. There was no radiographic evidence of activity. The patient was discharged symptom free on April 30, 1947. He has not returned to the clinic since that time.

DISCUSSION

Symptoms of spinal injury, characterized chiefly by severe back pain, muscle spasm over the lumbar area, tenderness over the lumbar spine, and difficulty in bending, stooping, or lifting, may occur immediately or as long

as six months after lumbar puncture (see Table I). Milward and Grout[12] reported one case occurring six months after lumbar puncture for spinal anesthesia. Pease[10] reported several cases occurring immediately following spinal puncture and others with onset of symptoms as long as two weeks later. In general, the earlier onset appears to occur in younger individuals, although in the cases reported by Deming and Zaff[14] the patients were 65 and 71 years old, respectively, with onset of symptoms five days and two weeks following spinal anesthesia. Stump and Narins[18] reported a case of a 12-year-old patient who did not have onset of symptoms until five months following lumbar puncture.

On a theoretical basis, one would expect onset of symptoms to occur more rapidly in children where the volume and fluid state of the nucleus pulposus is greater than in older patients. However, the amount of trauma and the site of trauma probably play a significant role in the time necessary for manifestation of the symptoms. Therefore, it is probably not the age but the type and extent of injury caused by the puncture needle that determines the rapidity with which the spondylitis develops. The statement is made in the literature that there is a longer latent period in cases of lumbar puncture for purposes of spinal anesthesia than in those performed for diagnostic or therapeutic aims. Analysis of reported cases, however, does not bear this out (see Table I). It is apparent that the type and extent of the injury is again the important factor regarding the onset of the symptoms and not whether the puncture was for diagnostic, therapeutic, or anesthetic purposes.

Radiographic evidence of spinal injury has been reported occurring as early as eighteen days (Findlay and Kemp[7]) to as late as six months (Everett[15]) after lumbar puncture. In the majority of cases, x-ray changes were in evidence within three to four months. Initially only a slight erosion of the articular surfaces may be seen (Milward and Grout[12]) but complete involvement of the entire joint subsequently occurs. As mentioned earlier in this paper, the most common x-ray findings are: (1) thinning of the intervertebral disc, (2) narrowing of the space between the respective vertebral arches and the intervertebral facets, (3) sclerosis of adjacent vertebral bodies, (4) rarefaction and destruction of the vertebral bodies. Pease[10] also reports compensatory widening of the intervertebral space above the affected one.

Treatment of spinal injury following lumbar puncture depends on the presence or absence of infection. If the injury gives rise to an inflammatory spondylitis due to the penetration of nuclear material into the spongiosa of adjacent vertebrae and there is no evidence of osteomyelitis, immobilization of the involved portion of the spine is all that is necessary. In all cases treated by proper immobilization by plaster body jacket (or Taylor brace later in the course), the patient recovered without incident. Everett[15] reported the cases of three patients, two of whom were treated by immobilization with improvement. The third was not immobilized and remained unimproved for six months.

If osteomyelitis of the spine is the consequence of traumatic lumbar puncture, antibiotic therapy in addition to immobilization is necessary. Healing is

TABLE II

PATIENT	REASON FOR LUMBAR PUNCTURE	ONSET OF SYMPTOMS (TIME SINCE LUMBAR PUNCTURE)	APPEARANCE OF RADIOGRAPHIC EVIDENCE (TIME SINCE LUMBAR PUNCTURE)	TREATMENT	RESULT
M. A. (33-year-old white man)	Diagnosis	7 weeks	9 weeks	Immobilization of spine, antibiotics	Complete healing
G. K. (67-year-old white man)	Spinal anesthesia	5 months	5 months	Bed rest on bed boards, antibiotics, immobilization of spine with back brace	Improvement in symptoms; patient died before further roentgenograms to determine state of healing could be obtained
M. G. (2-month-old white male infant)	Diagnosis	Not known	2 months	Antibiotics	Steadily downhill with temperature to 40° C.; patient died three weeks after admission
J. F. (61-year-old white man)	Spinal anesthesia	2 months	2 months	Antibiotics	Metastatic osteomyelitic focus, to right tibia; complete healing in spine and tibia; many recurrent abscesses of back, even after healing in spine

manifested by obliteration of the intervertebral joint space and bony bridging between the involved vertebral bodies.

The case of Goldenberg and Brooks[22] included in this series as a complication following lumbar puncture did not involve the vertebral bodies. The patient developed severe back pain three days after a difficult lumbar puncture. Roentgenograms thirty-two days after the puncture revealed rarefaction and early destruction of the spinous process of L_5. This continued to extensive necrosis of the spinous process which was removed at operation.

It is noteworthy that in almost all of the reported cases spinal injury followed difficulty with the lumbar puncture. It cannot be said that all cases followed difficult lumbar puncture only because several authors failed to mention the difficulty or ease with which the puncture was performed. If there is difficulty in obtaining fluid at any one level, the operator should proceed to the space above or below rather than continue to traumatize the spinal structures at the original level.

SUMMARY

1. Fifty-three cases of spinal injury following lumbar puncture are reviewed. (A case is included in which there was involvement of the spinous process rather than the vertebral body.)

2. Four additional cases (two from the Hospital for Special Surgery and two from The New York Hospital) are reported.

3. Symptoms of injury of the spine may occur immediately or as long as six months after the lumbar puncture.

4. In most of the cases intervertebral disc or vertebral injury occurred following difficult spinal puncture.

5. Radiographic changes are characterized chiefly by thinning of the intervertebral disc and sclerosis, rarefaction, and destruction of the vertebral body. These changes may occur from as early as eighteen days following the puncture to as long as six months after the puncture.

6. The type and extent of the injury caused by the puncture needle is more important in regard to the rapidity of the onset of the symptoms than is the age of the patient or the purpose of the puncture.

7. Treatment of the condition consists essentially in proper immobilization of the spine supplemented by antibiotic therapy if osteomyelitis develops.

8. Emphasis is made of the necessity for sterile technique and careful introduction of the needle in performing lumbar punctures. Utilization of a different level should be practiced if spinal fluid is not obtained easily at the original puncture site.

REFERENCES

1. Quincke, H.: Verhandl. d. Cong. f. innere Med., wiesb. **10**: 321, 1891.
2. Dripps, R. D., and Vandan, L. D.: J. A. M. A. **147**: 12, 1951.
3. Weed, L. H., Wegforth, P., Ayer, J. B., and Felton, L. D.: J. A. M. A. **72**: 190, 1919.
4. Levy, I. I., and Cohen, A. E.: J. A. M. A. **85**: 1968, 1925.
5. Symonds, C. P.: Lancet **1**: 434, 1925.
6. Billington, R. W.: J. A. M. A. **83**: 683, 1924.
7. Findlay, L., and Kemp, F. H.: Arch. Dis. Childhood **18**: 102, 1943.
8. James, U.: Proc. Roy. Soc. Med. **39**: 134, 1946.
9. Bromley, L. L., Craig, J. L., and Kessel, A. W. L.: Brit. M. J. **1**: 132, 1949.
10. Pease, C. N.: Am. J. Dis. Child. **49**: 849, 1935.
11. Gellman, M.: J. Bone & Joint Surg. **22**: 980, 1940.
12. Milward, F. J., and Grout, J. L. A.: Lancet **2**: 183, 1936.
13. Keyes, D. C., and Compere, E. L.: J. Bone & Joint Surg. **14**: 897, 1932.
14. Deming, C. L., and Zaff, F.: Tr. Am. A. Genito-Urin Surgeons **35**: 287, 1943.
15. Everett, A. D.: Proc. Roy. Soc. Med. **35**: 208, 1942.
16. Epps, P. G.: Proc. Roy. Soc. Med. **35**: 220, 1942.
17. Stewart, V. A. F., and Owen, A.: Med. J. Australia **2**: 295, 1943.
18. Stump, J. P., and Narins, S. A.: U. S. Nav. M. Bull. **41**: 400, 1943.
19. Martin, P.: Brit. M. J. **2**: 688, 1946.
20. Baker, A. H.: Brit. J. Surg. **34**: 385, 1947.
21. Brown, R., and Hoffman, B. P.: Bull. U. S. Army M. Dept. **8**: 391, 1948.
22. Goldenberg, R., and Brooks, S.: J. M. Soc. New Jersey **46**: 466, 1949.

EXTENDING THE ZONE OF RESECTION FOR CARCINOMA OF THE RECTUM AND SIGMOID

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THIS discussion intends to emphasize the radical removal of proximal lymphatic draining areas in nonpalliative resection for invasive carcinoma of the rectum and left colon, a technical concept which should conform to the fundamental surgical principle of wide resection of a primary malignant lesion with the regional lymphatic channels and nodes in continuity, whenever possible. It appears that this principle has been neglected in resection of the rectum and sigmoid, for reasons to be presented later.

Early radical surgery for cancer in these areas yields gratifying results as compared with that performed for similar lesions elsewhere in the gastrointestinal tract. It would seem, therefore, that still better results would be obtained by increasing the zone of lymphatic resection for curable lesions in the rectum and colon. Most surgeons agree that the classical abdominoperineal resection is the preferred surgical treatment for carcinoma of the rectum at or below the reflection of the pelvic pertioneum, because it removes the lateral and inferior and superior zones of lymphatic spread. Above this level, most believe that anterior resection and anastomosis may be carried out, provided the bowel is divided two or more inches below the lesion and the lymphatic-bearing area of mesentery is removed. Further, it is generally conceded that contiguous organs which may be involved, such as uterus, tubes, ovaries, prostate, bladder, small intestine, abdominal wall, and ureter should often be excised en bloc when resection is performed for cure.

Much has been written—and there is general agreement—on the extent of resection which should be performed in the vicinity of and below malignant lesions in this segment of the intestine; but little has been said, and it appears there is no widespread opinion or practice, regarding the acceptable *upper limits of excision*. To most of us an acceptable upper point of resection should be the highest possible excision of the mesentery with attached colon, namely, the upper limits of the inferior mesenteric vessels.

However, from observation and perusal of surgical textbooks and monographs, it would appear that such a point has not been the favored upper line of excision. For instance, Gabriel,[1] of England, a direct pupil of Sir Earnest Miles, recently described the upper limit for division of the inferior mesenteric artery for carcinoma of the rectum at a point below the first sigmoid branch. Rankin and Graham,[2] in the 1950 edition of their book, illustrate the inferior

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mesenteric artery ligated at the level of the sacral promontory for the same operative procedure. Colcock and Mace,[3] recently discussing the same subject, stated: "Since the main nodal spread is along the inferior mesenteric artery, it should be divided at least as high as the bifurcation of the aorta." It is fully appreciated that material in textbooks and monographs, right or wrong, may not be in accord with current practice. Further, it is probable that many in the past have realized the need for higher lymphatic resection, but have been reluctant to practice it because of fear of an increased mortality for an already extensive procedure. Assuming, however, that the most extensive and effective resection for carcinoma in these areas is not in general use, one may next logically ask whether or not it would be desirable, feasible, and fruitful to encourage expansion of an already extensive operative procedure. From what we know of the anatomy and lymphatic spread and resectability of these lesions, it would seem that this would be true.

LYMPHATIC SPREAD

Extension of the lymphatic and nodal chain from the rectum and sigmoid up to and above the origin of the inferior mesenteric vessels is an anatomic fact. To quote from the 1948 edition of Gray's Anatomy[4]: "Lymph vessels of the rectum and lower sigmoid traverse the pararectal glands upward to those in the mesocolon terminating in the pre-aortics around the origin of the inferior mesenteric artery." Sir Earnest Miles, in 1908, being aware of the extent of the lymphatic drainage area of the rectum and sigmoid, described the radical operation for carcinoma of the rectum which bears his name. Many details, however, regarding mechanism and incidence of regional lymphatic metastases have been determined since that time which have produced our present concept of the problem. Villemin and Huard[5] described three types of lymph channel drainage from the rectum: (A) short vessels which penetrate the bowel wall and communicate with the pararectal glands of Gerota, (B) medium channels which by-pass the pararectal glands and terminate in the mesocolic group, and (C) lymphatics which extend all the way from the bowel wall to a small group of glands near the origin of the inferior mesenteric aretry near the left colic branch. This work was confirmed later both by Gabriel and associates[6] and by Oliveira.[7] During the same period, Gabriel and associates,[6] Gilchrist and David,[8] and Coller and associates,[9] after study of resected specimens, determined that the spread from these lesions occurred in an orderly pattern in the great majority of instances, that is, from the lesion to pararectal and from pararectal to mesocolic and thence to higher paraaortic nodes. They also demonstrated that an involved node usually prevents further spread until the node itself is replaced by metastases. Much of the logic regarding extensive block resection for carcinoma is based on this observation. In addition, these three groups of investigators also observed occasional instances of disorderly spread: that is, involvement of nodes just below the left colic artery without intermediate metastases, and similar involvement of lower mesocolic nodes without metastases to Gerota's glands.

The importance regarding the possibility of such high lymphatic involvement in patients operated upon for cure may be amplified by the observations of Gilchrist and David.[8] They examined eleven patients who died from incidental illnesses during the immediate postoperative period following abdominoperineal resections for carcinoma. Four of these patients showed remaining nodal involvement approximately two inches above the upper limit of resection and with no metastases to more proximal nodes or liver. They concluded that the widest possible resection of the upper mesocolon be carried out in all cases of carcinoma of the rectum and sigmoid. Dukes[10] came to the same conclusion after studying his Group "C" cases which he had divided into two subgroups: "C_1" and "C_2"—C_1 being cases with only nodes

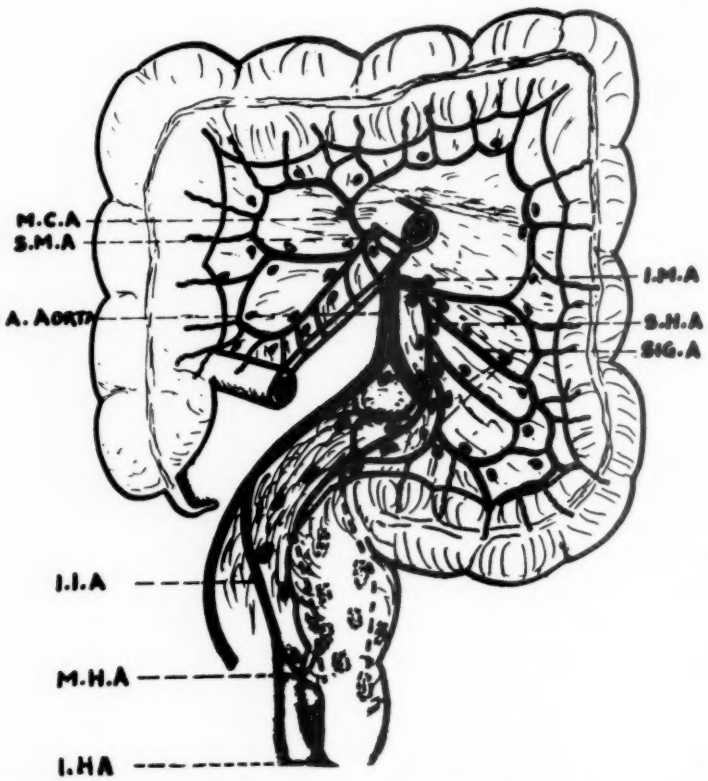

Fig. 1.—A diagrammatic representation of the arterial blood supply to the colon and rectum indicating the usual lymph node distribution (redrawn from Singleton).

proximal to lesions involved, and C_2 those cases where nodal metastases extended to or occurred at the point of upper arterial ligation. As might be expected, he noted a considerable difference in outlook for cure between these two groups. It is important for our purpose to note that involvement of *nodes in the vicinity of the origin of the left colic artery* does occur, either as the ultimate result of orderly spread from intervening glands or from metastatic emboli direct from the rectal or sigmoidal lesion. The significance of these observations and conclusions regarding lymphatic spread from carcinoma in these

areas becomes important when we consider that the present survival rate for patients with nodal involvement is only 40 per cent, and, of course, any suggestion which might improve this figure would be welcome.

ANATOMIC CONSIDERATIONS

If one concedes the desirability of more radical upward resection for carcinoma in the lower intestine, it is next logical to ask whether this can be done with safety. The experimental work of Sudeck,[11] in 1907, resulted in the designation of a so-called "critical point" for ligation of the superior hemorrhoidal artery which would insure a safe blood supply for the proximal

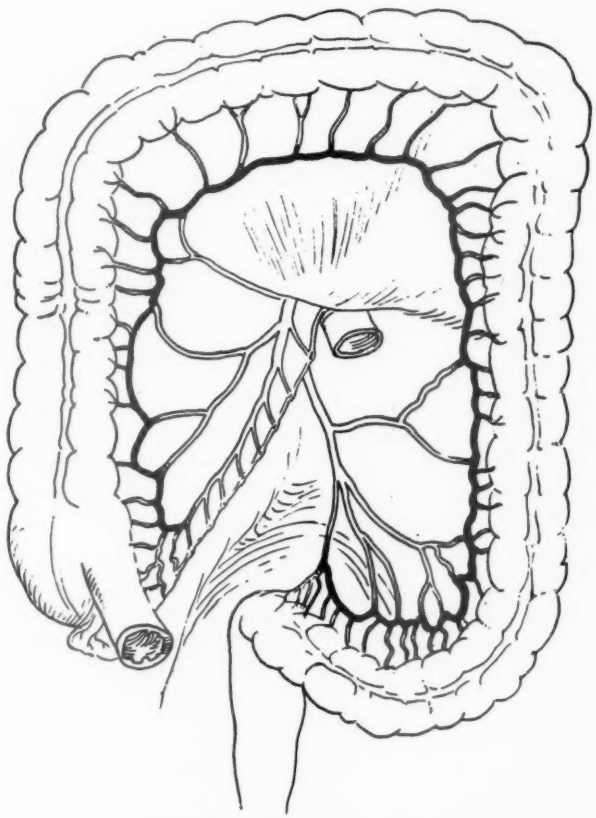

Fig. 2.—Blood supply of the colon and rectum showing the marginal artery of Drummond indicated by solid black lines.

segment. In this respect, Ault and associates[12] have appropriately emphasized that Sudeck's work was concerned with the problem in relation to *perineal resection of the rectum,* since abdominoperineal resection with terminal colostomy and anterior resection were not in significant use until after 1908. Certainly Sudeck's work has influenced to some extent the surgical teaching and, coincidentally has limited the upper extent of resection for the past forty years.

Excellent surgical anatomic studies have been undertaken, particularly in the past two decades, which demonstrate the safety and propriety of ligation

of the inferior mesenteric artery, in most cases at a much higher level, in the course of resection for cancer of the rectum and sigmoid. Pope and Judd,[13] in 1929, decided that ligation at the level of sacral promontory for the abdominoperineal resection was appropriate without emphasizing Sudeck's critical point. Steward and Rankin,[14] in 1933, and Sunderland,[15] in 1942, focused attention on the presence of marginal vessels which, in most cases, communicated freely with the middle and left colic systems, rendering it possible to ligate above the first sigmoidal branches. Subsequent and quite recent studies by Bacon and associates[16-18] have confirmed these findings. These latter surgeons in developing their "pull through" technique for carcinoma of the rectosigmoid have decided that Sudeck's point may be ignored in resections for carcinoma of the rectum and rectosigmoid. They found in the course of 146 consecutive resections for carcinoma of the rectosigmoid that, by careful preservation of the marginal communicating arcades, the upper sigmoid could be transferred to the anus without impairment of terminal blood supply. Further, Goligher[19] applied the principle of high mesenteric arterial ligation directly to the Miles operation and to anterior resection, emphasizing the dependability, in most cases, on the presence of the marginal artery to provide blood to the distal sigmoid, if needed. Singleton[20] reported that a break in the continuity of the marginal vessel was encountered in a few of his cases, which caused some concern regarding elective anastomosis; however, in each instance, this break merely required additional mobilization of proximal colon. Rather recently, Ault and associates[12] reviewed thirty-two cases of Miles-anterior, and Bacon resections. In five of these the inferior mesenteric artery was ligated at the aorta, the balance were ligated within two and one-fourth inches of its origin, a point approximately at the aortic bifurcation. Their work demonstrates the feasibility of high ligation proximal to the first sigmoid branch.

Concern regarding the adequacy of circulation in the rectal stump may be present in executing anterior resections. The blood supply in this instance comes from the internal iliac system and through the middle and inferior hemorrhoidal vessels. Free anastomosis between these two sources almost invariably exists. When the middle hemorrhoidals are small or must be severed with the lateral ligaments, one can usually still be assured of adequate blood supply from the inferior vessels. Dixon,[21] in 1944, while developing his technique for anterior resection for carcinoma of the rectum, encountered no vascular deficiency complications at the site of low anastomosis after sacrificing the superior hemorrhoidal artery in 100 consecutive cases. It would seem, therefore, that one need not limit the extent of resection for cancer in the rectum and sigmoid on purely anatomic grounds.

CASE STUDIES

It became our general policy late in 1950 to execute all nonpalliative resections for carcinoma of the rectum and sigmoid in the following manner whenever possible:

For invasive carcinoma at or below the reflected pelvic peritoneum, a radical abdominoperineal resection was carried out by: (1) wide mobilization of the rectum including all pararectal tissue, (2) incision of the lateral parietal peritoneum upward and freeing of the lienocolic and left lateral portion of the gastrocolic ligaments to provide extensive mobilization of the splenic flexure and descending colon, (3) ligation of the inferior mesenteric artery just proximal to the left colon artery or just distal to it when the latter had arisen close to the origin of the former, (4) ligation of the inferior mesenteric vein as high as possible with removal of all distal mesentery laterally to the marginal vessels, (5) creation of the terminal colostomy at about the

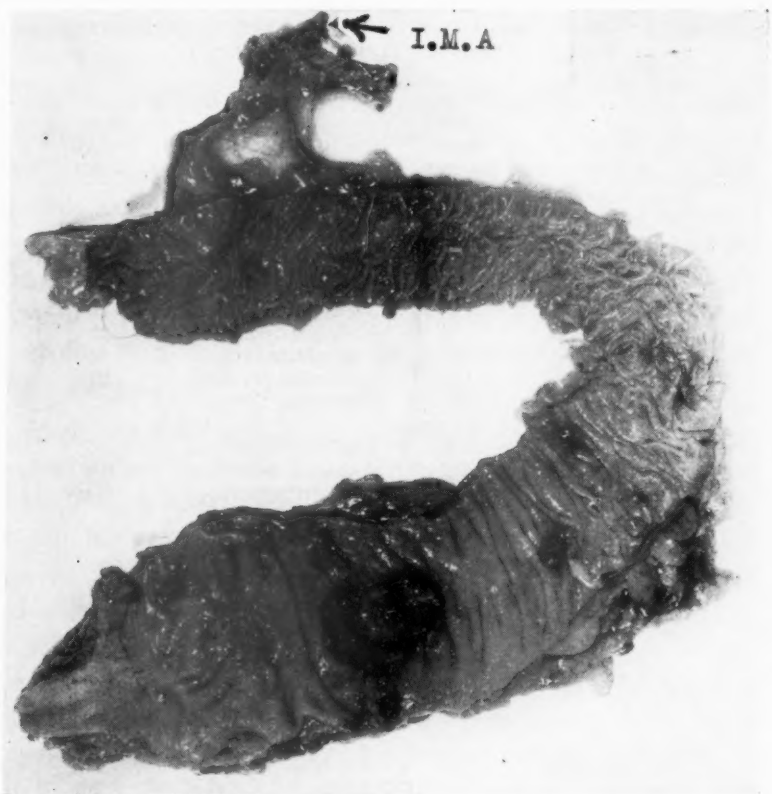

Fig. 3 (Case 5).—Excised specimen of anus, rectum, and sigmoid showing point of inferior mesenteric ligation.

junction of descending colon and sigmoid or more proximal if there was question regarding viability, (6) execution of the balance of the procedure as usual with wide perineal and levator excision, particularly if the lesion was in the lower one-half of the rectum.

For lesions lying entirely within the peritoneal cavity, the usual choice was anterior resection with open end-to-end anastomosis in the following manner: (1) the splenic flexure and descending colon were mobilized followed by ligation of the inferior mesenteric vessels, followed by wide mesentery

excision as previously indicated, (2) all lymphatics with vessels and mesentery were dissected downward from the surface of the aorta, vena cava, sacrum, and lateral pelvic walls to a point at least two inches below the lower border of the lesion, (3) the bowel and attached mesentery were then cut off below and at a point above the lesion to include the entire area of lymphatic drainage, or higher, (4) open anastomosis was then executed between viable segments of intestine. Since September, 1950, twenty consecutive nonpalliative resections of the sigmoid and rectum have been executed according to this plan and are listed in Table I. There have been no deaths, and operating time and morbidity have not been increased.

TABLE I. TWENTY CONSECUTIVE NONPALLIATIVE OPERATIONS FOR CARCINOMA OF THE RECTUM AND SIGMOID IN WHICH HIGH LIGATION OF THE INFERIOR MESENTERIC ARTERY WAS AN EXECUTED TECHNICAL PRINCIPLE*

CASE	AGE (YEARS)	LOCATION OF LESION	PATHOLOGIC GROUP (DUKES)	OPERATIVE PROCEDURE	HOSPITAL DAYS	COMPLICATIONS
1	48	Low sigmoid	A	Anterior resection	11	None
2	30	Rectum	B	Abdominoperineal resection	16	None
3	45	Rectum	C	Abdominoperineal resection	21	None
4	42	Mid sigmoid	B	Anterior resection	10	None
5	56	Rectum	B	Abdominoperineal resection	23	Urinary retention
6	51	Rectum	C	Abdominoperineal resection	21	Urinary retention
7	55	Upper sigmoid	B	Anterior resection	15	None
8	60	Upper sigmoid	B	Anterior resection	16	None
9	51	Rectum	C	Abdominoperineal resection	24	None
10	56	Rectum	C	Abdominoperineal resection	21	None
11	51	Rectum	C	Abdominoperineal resection	27	Prolonged ileus
12	65	Rectum	B	Abdominoperineal resection	18	None
13	48	Low sigmoid	C	Anterior resection	14	None
14	53	Rectum	B	Abdominoperineal resection	39	Postoperative coronary occlusion
15	58	Rectosigmoid	C	Anterior resection	15	None
16	52	Rectum	C	Abdominoperineal resection	19	None
17	45	Rectum	B	Abdominoperineal resection	18	None
18	48	Rectosigmoid	B	Anterior resection	15	None
19	49	Mid sigmoid	C	Anterior resection	14	None
20	49	Low sigmoid	C	Anterior resection	21	None

*Seven of these patients were operated upon by Dr. J. E. Strode, the rest by the author.

Conceivable limitations or contraindications to the procedure have occurred to us, as already indicated in the reports of Ault, Castro, and Smith,[22] such as the possibility that (1) substandard-risk patients might not tolerate the additional upward dissection and mobilization of the intestine, or (2) the presence of a short, thick, fatty mesentery or one diffusely filled with metas-

tases might render dissection too hazardous, particularly in patients with a low duodenojejunal junction. So far we have not encountered any of these obstacles.

COMMENT

The idea concerning emphasis of a more radical approach to lesions of the rectum and left colon is by no means new or original. Maes and Essrig,[23] in 1949, concluded from their experience that the higher curability rate for right colon lesions might be due to the larger amount of mesentery and nodes which must of necessity be removed, and that it would be reasonable to expect hemicolectomy on the left to result in a higher curability rate for lesions in the rectum and sigmoid. Karl Meyer[24] has advocated left hemicolectomy for these lesions, without reservation. Quite recently, Ault, Castro, and Smith[22] published the results of their exhaustive study of this problem. During the preparation of this manuscript, Ariel[25] has emphasized this technical policy in his institution—also, Grinnell and Hiatt,[26] in a series of forty-one resections utilizing this principle, have concluded that the operation is inadequate if this higher resection is not performed. Much more investigative work concerning this problem must be done. Specimens removed by this method should be examined carefully for lymphatic and nodal involvement, particularly in areas near the upper extent of the inferior mesenteric artery and along the upper extensions of the vein, to determine the frequency with which high local extension might occur.

Apart from the desirability of the widest possible local and regional resection for carcinoma in these areas, one must also consider the small group of individuals who develop subsequent primary carcinomas or adenomas when portions of the sigmoid remain. It is also good surgery to remove "cancer soil" whenever feasible. No honest surgeon would execute a radical operation for carcinoma of the breast without removing the lymphatic elements in the apex of the axilla along with the pectoral structures, at least as high as the mid-point of the clavicle at the chest wall. It seems analogous and reasonable that high ligation of the inferior mesenteric artery with resection of the adjacent mesentery and bowel should likewise be the standard or acceptable upper limit of resection for malignancy in the lower colon and rectum. As stated earlier, the logic of resecting lymphatic drainage areas at the most proximal point is based on our knowledge that spread to higher nodes usually does not occur unless lower nodes are completely involved. By high ligation of the inferior mesenteric vessels and excision of adjacent mesentery, one hopes to cure a larger percentage of those cases where spread to the mesocolic nodes only has occurred.

SUMMARY AND CONCLUSIONS

1. Investigations regarding the lymphatic spread of carcinoma of the sigmoid and rectum during the past forty years suggest that the highest, widest and often lowest possible resection of the lesion and lymphatic-drain-

age area must be resected if high curability rates are to be expected, particularly in the group with nodal involvement.

2. High resection of the mesentery and upper lymphatic spread is possible only when the inferior mesenteric artery is ligated at, or very near, its origin from the aorta, and the mesenteric vein is resected as high as possible.

3. Such high ligation of upper blood supply appears to be compatible with adequate terminal colostomy or with availability of viable bowel for anterior resection and anastomosis, in most instances, due to the free communication of the superior and inferior mesenteric vascular systems and to the abundant blood supply to the lower rectum through the middle and inferior hemorrhoidal vessels.

4. This technique is an actual routine in many surgical centers. Our own experience with the procedure in twenty cases has been gratifying, providing a sense of satisfaction that the malignancy has been dealt with as completely as possible without producing increased mortality and morbidity.

5. We believe with many others that the so-called "critical point" of Sudeck should be ignored or de-emphasized. Surgeons should concern themselves first with thorough wide resection of these neoplasms and the lymphatic draining area, followed by evaluation and reconstruction of the defect in accordance with sound surgical principles.

ADDENDUM

The case series indicated in Table I had by March 30, 1953, been extended to twenty-nine with consistent results.

REFERENCES

1. Gabriel, W. B.: Perineo-abdominal Excision of Rectum in One Stage, Am. J. Surg. **79**: 76, 1950.
2. Rankin, F. W., and Graham, A. S.: Carcinoma of the Colon and Rectum, ed. 2, Springfield, Ill., 1950, Charles C Thomas, Publisher, p. 370.
3. Colcock, B. P., and Mace, A. J.: Choice of Operative Procedure in the Treatment of Carcinoma of the Colon and Rectum, Lahey Clin. Bull. **7**: 139, 1951.
4. Gray's Anatomy, Philadelphia, 1948, Lea & Febiger, p. 722.
5. Villemin, F., Huard, P., and Montagne, M.: Cited by Bacon, H. E., and Sauer, J.: Selection of Surgical Procedure in Treatment of Cancer of the Rectum, J. Internat. Coll. Surg. **13**: 24, 1950.
6. Gabriel, W. B., Dukes, W. C., and Bussey, H. J.: Lymphatic Spread in Carcinoma of the Rectum, Brit. J. Surgeons **23**: 395, 1935.
7. Oliveira, E.: Observacão sobre os linfatices anorectais, Rio de Janeiro Tese, p. 77, 1947. Cited by Bacon, H. E., and Sauer, J.: Selection of Surgical Procedure in Treatment of Carcinoma of the Rectum, J. Internat. Coll. Surg. **13**: 24, 1950.
8. Gilchrist, R. K., and David, V. D.: Prognosis in Carcinoma of the Bowel, Surg., Gynec. & Obst. **86**: 359, 1948.
9. Coller, F. A., Kay, E. B., and MacIntyre, R. S.: Regional Lymphatic Metastasis of Carcinoma of the Rectum, SURGERY **8**: 294, 1940.
10. Dukes, C.: Rectal Cancer, Tr. Am. Proct. Soc. 66, 1950.
11. Sudeck, P.: Ueber de Gefässversorgung des Mastdarmes in Hinsicht auf die operative Gangrän, München. med. Wchnschr. **54**: 1514, 1907. Cited by Ault.[21]
12. Ault, G. W., Castro, A. F., and Smith, R. F.: Carcinoma of Upper Rectum and Rectosigmoid, Postgrad. Med. **8**: 176, 1950.
13. Pope, C. E., and Judd, E. S.: The Arterial Blood Supply of the Sigmoid, Rectosigmoid, and Rectum, S. Clin. North America **9**: 957, 1929.

14. Steward, J. A., and Rankin, F. W.: Blood Supply of Large Intestine; Its Surgical Considerations, Arch. Surg. **26**: 843, 1933.
15. Sunderland, S.: Blood Supply of the Distal Colon, Australian & New Zealand J. Surg. **11**: 253, 1942.
16. Bacon, H. E., and Rowe, R. J.: Radicability of Methods to Eliminate Colostomy; Critical Review, J. Internat. Coll. Surgeons **11**: 243, 1948.
17. Bacon, H. E., and Smith, C. H.: Arterial Supply of Distal Colon Pertinent to Abdominoperineal Proctosigmoidectomy With Preservation of Sphincter Mechanism, Ann. Surg. **127**: 28, 1948.
18. Bacon, H. E.: Cancer of the Rectum, SURGERY **26**: 584, 1949.
19. Goligher, J. C.: Blood Supply to the Sigmoid Colon and Rectum, Brit. J. Surg. **27**: 157, 1949.
20. Singleton, A. O.: The Blood Supply of the Large Bowel With Reference to Resection, SURGERY **14**: 328, 1943.
21. Dickson, C. F.: Anterior Resection for Carcinoma Low in the Rectosigmoid, SURGERY **15**: 367, 1944.
22. Ault, G. W., Castro, A. F., and Smith, R. S.: Clinical Study of Ligation of the Inferior Mesenteric Artery in Left Colon Resections, Surg., Gynec. & Obst. **94**: 223, 1952.
23. Maes, U., and Essrig, J. M.: Surgical Principles on Treating Carcinoma of the Colon and Rectum, Ann. Surg. **130**: 1008, 1949.
24. Meyer, K. A.: Treatment of Carcinoma of the Left Colon by Hemicolectomy, Postgrad. Med. **10**: 403, 1951.
25. Ariel, I.: Treatment of Cancers of the Colon, Rectum and Sigmoid, Am. J. Proctol. **3**: 7, 1952.
26. Grinnell, R. S., and Hiatt, R. B.: Ligation of the Inferior Mesenteric Artery at the Aorta in Resections for Carcinomas of the Rectum and Sigmoid, Surg., Gynec. & Obst. **94**: 526, 1952.

A STAINLESS STEEL MESH PROSTHESIS FOR IMMEDIATE REPLACEMENT OF THE HEMIMANDIBLE

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AN INCREASING number of jaw resections are being performed for malignant disease. Consequently, numerous techniques for immediate or subsequent mandibular replacement have been described. This operation is indicated for benign and malignant tumors of the mandible, osteomyelitis, radiation necrosis, traumatic loss, or incidentally during en bloc dissections for tumors of contiguous tissues adjacent to or involving the mandible. In the resection of segments of the lower jaw, immediate fixation of the fragments is necessary to prevent deviation which results from unopposed muscle pull and scarring. Such displacement is not only disfiguring, but often results in feeding problems and respiratory distress.

The ideal replacement of resected portions of mandible is autogenous bone. New[11] advocated the use of iliac crest cut to the shape desired. Conway[6] preferred a rib graft fractured and bent at its mid-point to simulate the angle of the jaw. Marino and associates[10] devised an ingenious method, that of inserting cancellous bone chips from the ilium into the defect, and molding it from within with an acrylic intraoral splint and from without by a plaster cast to retain the shape of the mandible. It has been emphasized by Conway that, whenever possible, the condyle and upper portion of the ramus of the mandible should be preserved to facilitate reconstruction.

Immediate bone grafting is not always feasible. The mucosa of the mouth is often entered, introducing oral contamination which precludes successful grafting. If a considerable amount of mucous membrane is resected, the insertion of a graft may prevent satisfactory primary closure of the mucosa. In resection of the mandible for malignant tumors, immediate bone grafting is inadvisable; an adequate period of time must elapse to insure nonrecurrence before plastic repair is considered. In cases where large doses of irradiation are employed in the treatment of tumors, and sections of the mandible are resected for recurrent cancer or osteoradionecrosis, the radiation changes in the soft tissues prevent the use of an immediate bone graft.

After partial resection of the mandible, the displacement of the fragments may be prevented by fixation of the upper and lower jaws postoperatively. However, if no internal replacement is provided, there is loss of contour of the face, and later bone grafting is rendered difficult by contracture of the soft tissues. Furthermore, the retraction and fibrosis of the tissues will make it

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impossible to place the transplanted bone in proper relationship to the muscles of mastication. In order to maintain normal anatomic relationships, a variety of prosthetic appliances have been devised for temporary or permanent mandibular replacement. After extensive animal and chemical experiments, Venable and Stuck[14] demonstrated that three metals were sufficiently inert to be utilized in surgery. These are Vitallium, tantalum, and "18-8-SMO" stainless steel.

Byars[2] utilized ordinary steel pins to keep the mandibular fragments apart. Such pins or wires often become loosened or twisted, altering space relationships. Furthermore, fixation is not rigid and the pins occasionally protrude through the mucosa of the mouth. Byars[1] also used stainless steel bars between the bone ends with success. Freeman[7] used simple Sherman bone plates of varying lengths, bent to the proper curvature. Winter and associates[16] used a Vitallium plate for reconstruction of both horizontal rami of the mandible. It was necessary to remove the plate about one year later. Kleitsch[8] resected one-half the mandible, including the condyle, for malignant ameloblastoma and inserted a precast Vitallium prosthesis which included an artificial condyle. This does not appear necessary, as proper function of the jaw can be maintained by the temporomandibular joint on the healthy side. Conley[5] discussed in detail the use of Vitallium for mandibular replacement and for support of autogenous bone grafts. Ward and associates[15] inserted an acrylic prosthesis through the mouth, not imbedded in the tissues, to keep the fragments apart. Mucous membrane covered the defect in approximately six months.

The purpose of this paper is to report the use of an inexpensive, easily constructed, light, rigid prosthesis to replace nearly one-half of the mandible resected for an extensive ameloblastoma in a 13-year-old boy.

CASE REPORT

J. W., a 13-year-old Negro boy, was admitted to Maimonides Hospital on Dec. 9, 1951, with a history of swelling of the right jaw of nine months' duration. Past history was negative. He was in good health until April, 1951, when his friends noted that his right jaw was swollen. There was no history of trauma. Shortly after the swelling was noted, he began to complain of dull pain in the right lower jaw. This recurred intermittently for several weeks, but the pain finally subsided, although the swelling progressed gradually up to the time of admission. In August, 1951, he was admitted to another hospital where intraoral biopsy of the right mandible revealed ameloblastoma. Following this procedure, a persistent sinus developed on the alveolar margin just posterior to the molar region.

Physical Examination.—The patient was a well-nourished and normally developed Negro boy in no acute distress. There was marked asymmetry of the face due to diffuse swelling of the right one-half of the jaw (Fig. 1, *A*). The tumefaction involved the ascending ramus and most of the horizontal ramus of the right mandible. The skin overlying the bone was intact. The right lower alveolar margin was widened and there was a defect 1 cm. in depth behind the last molar tooth. There was no palpable cervical lymphadenopathy. The remainder of the physical examination was essentially negative.

Laboratory Data.—Red blood count was 4,100,000, hemoglobin 82 per cent, and white blood count 5,300 with normal differential. Urinalysis and blood Wassermann test were negative.

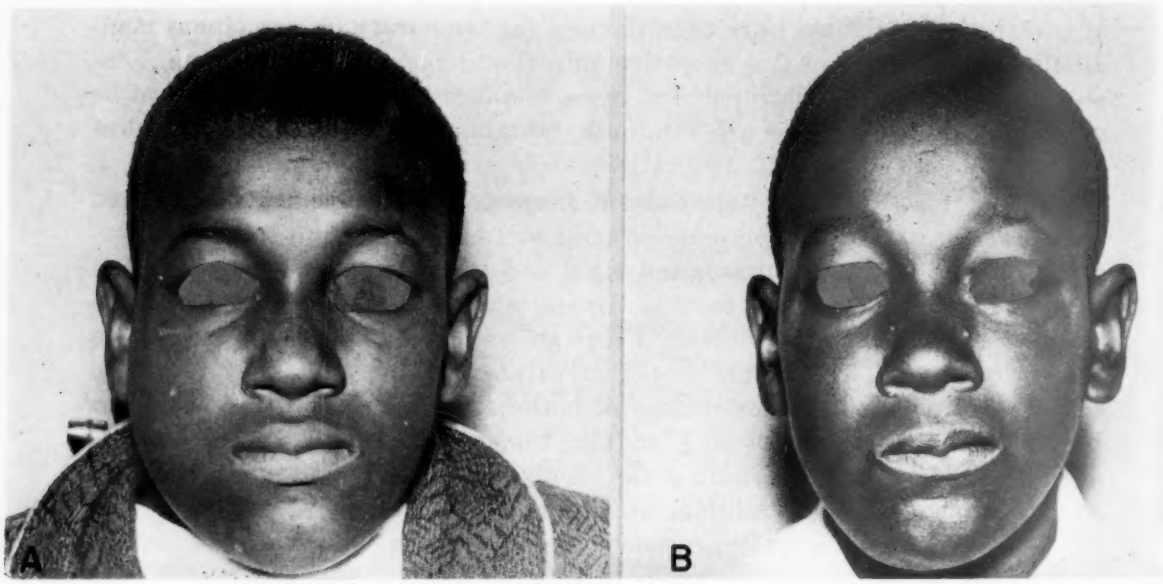

Fig. 1.—*A*, Preoperative review of patient. Note diffuse swelling of right jaw. *B*, Appearance five months after operation.

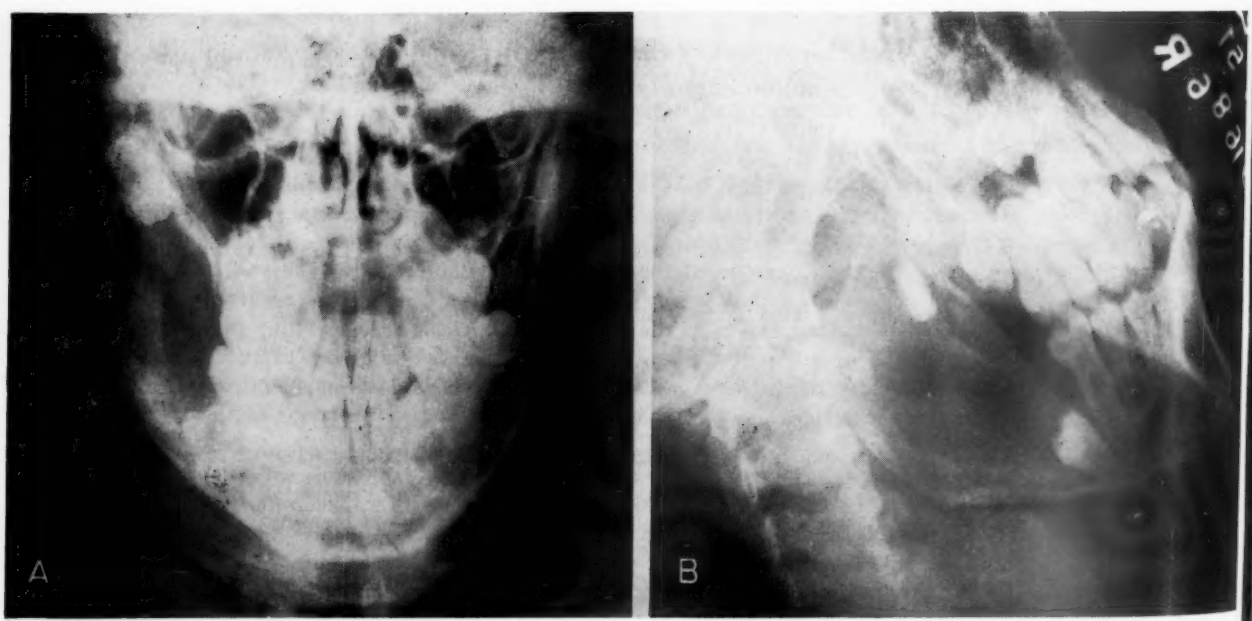

Fig. 2, *A* and *B*.—Preoperative roentgenograms demonstrating diffuse expansion and rarefaction of right one-half of mandible.

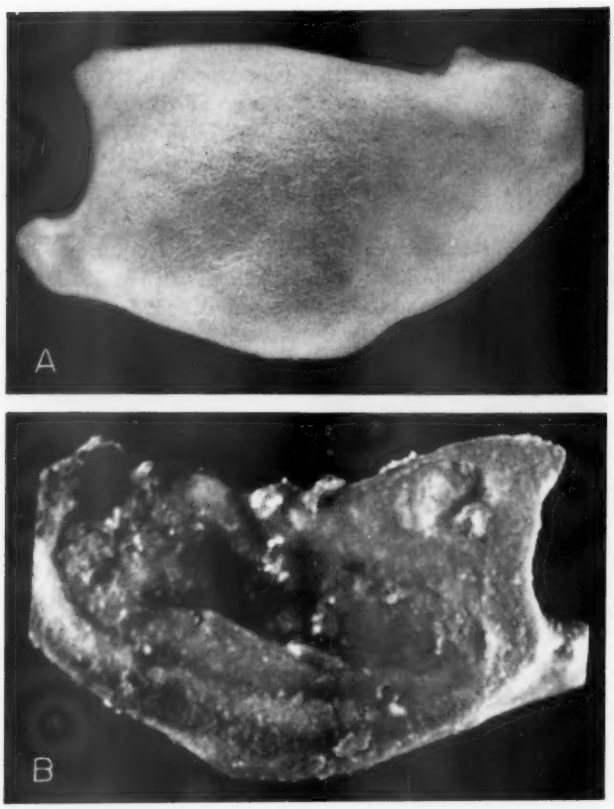

Fig. 3.—Resected portion of right mandible. *A*, Lateral view. *B*, Sagittal section through the bone showing a soft tissue mass within the substance of the mandible, extending to the base of the condyle.

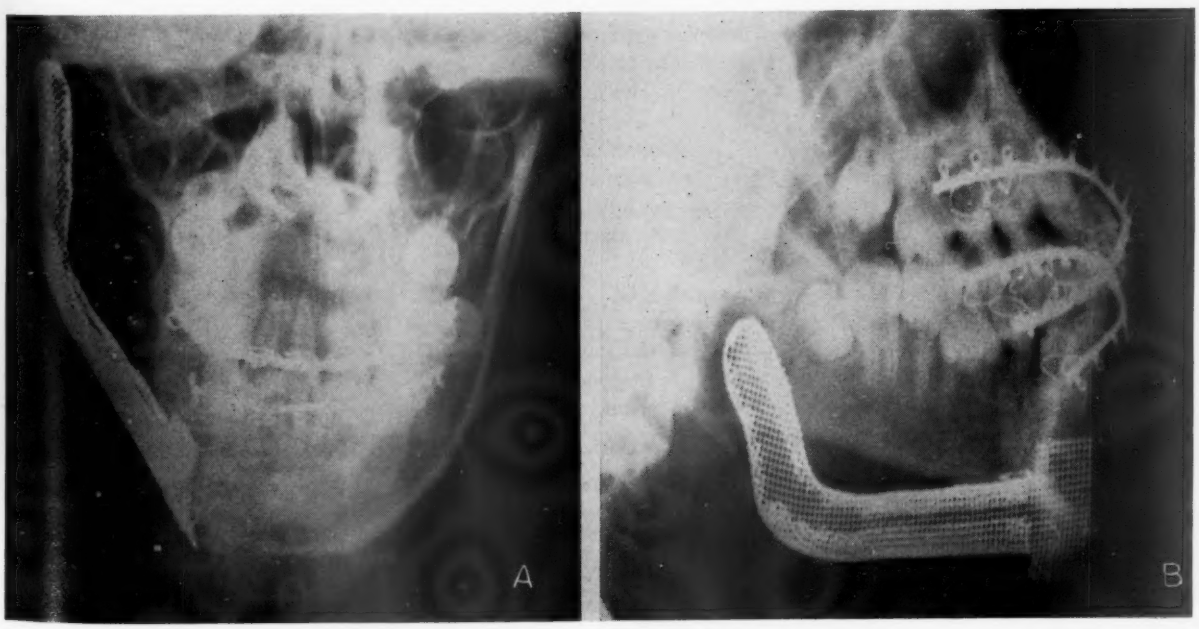

Fig. 4, *A* and *B*.—Postoperative roentgenograms, illustrating prosthesis in place, fixed to remaining mandible with wire sutures.

Roentgenologic Studies.—

Right mandible (Fig. 2): There was generalized expansion of the horizontal and ascending rami of the mandible, extending from the second premolar tooth to the neck of the condyle. There was diffuse ballooning out and rarefaction. No trabeculation was present. An impacted molar tooth was found within the cystlike area. The crown of the third molar was displaced toward the coronoid process.

Left mandible: The left mandible appeared normal. Chest x-ray examination was essentially negative.

Hospital Course.—Preoperatively, models of upper and lower jaws were prepared by the Dental Department, and Jelenko splints were placed in both jaws. Procaine penicillin G was administered during the twenty-four hours prior to operation.

The operation was performed on Dec. 17, 1951, under endotracheal anesthesia. The right one-half of the mandible was resected through a modified Kocher incision, from the level of the second premolar, including the condyle. The stainless steel mesh prosthesis was inserted and fixed to the mandible with wire sutures. The periosteum was sutured over the implant, and the wound was closed in layers.

At the termination of the operation the jaws were immobilized by attaching rubber bands to the Jelenko splints. A No. 18 whistle-tip catheter was inserted into the esophagus through the nose for feeding.

Pathologic Report.—

Gross: The specimen consisted of the body and ramus of the right mandible, including the condylar and coronoid processes (Fig. 3, *A*) measuring 10 by 5 by 3 cm. The alveolar border presented a soft, tannish gray mass which projected above the surface of the bone for a distance of 1 cm. Sagittal section through the bone (Fig. 3, *B*) revealed a soft tissue mass expanding within the substance of the bone, the entire mass measuring 5.5 by 2.5 cm. The surface for the most part was grayish white with scattered hemorrhagic areas. In one portion of the mass, a spicule of bone appeared to be entirely surrounded by the tumefaction.

Microscopic: Sections revealed cords or nests of epithelial cells embedded in an edematous connective tissue stroma. The centers of the masses revealed cystic formation, the periphery of which was covered with a single layer of cuboidal cells. The cells of the nests were hyperchromatic and small with scant cytoplasm, and the nuclei were oval or round and uniform. No mitotic figures were noted. The epidermis in many areas revealed acanthosis. Extensive areas of necrosis were noted. Sclerosis was also a prominent feature.

Diagnosis.—Ameloblastoma (adamantinoma) of right mandible.

Postoperative Course.—The patient was ambulated on the first day postoperatively. The temperature rose to 101° F. on the evening following operation, but gradually fell to normal by the fourth day. The cutaneous sutures were removed on the sixth day, the wound healing per primam. Nasal feedings were administered for ten days, at which time oral feedings were begun. Procaine penicillin G, 600,000 units daily, was given for five days postoperatively. The patient was discharged on Dec. 29, 1951, twelve days after operation.

Intermaxillary fixation was continued for a period of ten weeks, at which time the splints were removed and active motion of the jaws was permitted. Postoperative roentgenograms revealed normal position of the implant (Fig. 4). At the time of last examination on May 31, 1952, facial contour was good and there was full range of motion of the jaws (Fig. 1, *B*). The teeth were in normal occlusion. On palpation, the prosthesis was rigid and well fixed to the mandible.

DISCUSSION

Ameloblastoma (Adamantinoma).—This epithelial tumor arises from the odontogenic apparatus from cells with the potentiality for forming tissues of the enamel organ. It occurs most frequently in the mandible, but may be found in the maxilla, and rarely in the tibia. It is a slow-growing, relatively

benign tumor, but with continued growth it can produce tremendous destruction with considerable deformity and suffering. In a review of 379 cases, Robinson[12] found 4.5 per cent to be malignant. Furthermore, in about one-third of the cases there was recurrence one to twenty-two times after treatment. The usual method of treatment has been curettage or enucleation. It was pointed out by Lubschitz[9] that early in the course of the disease the tumor extends into the lacunae of the bone and will recur unless the surrounding bone is resected. Since ameloblastomas arise in the alveolar ridge of the mandible, it should be possible to resect the involved area completely by marginal resection in early cases, leaving the lower margin of the bone intact.[13] In the

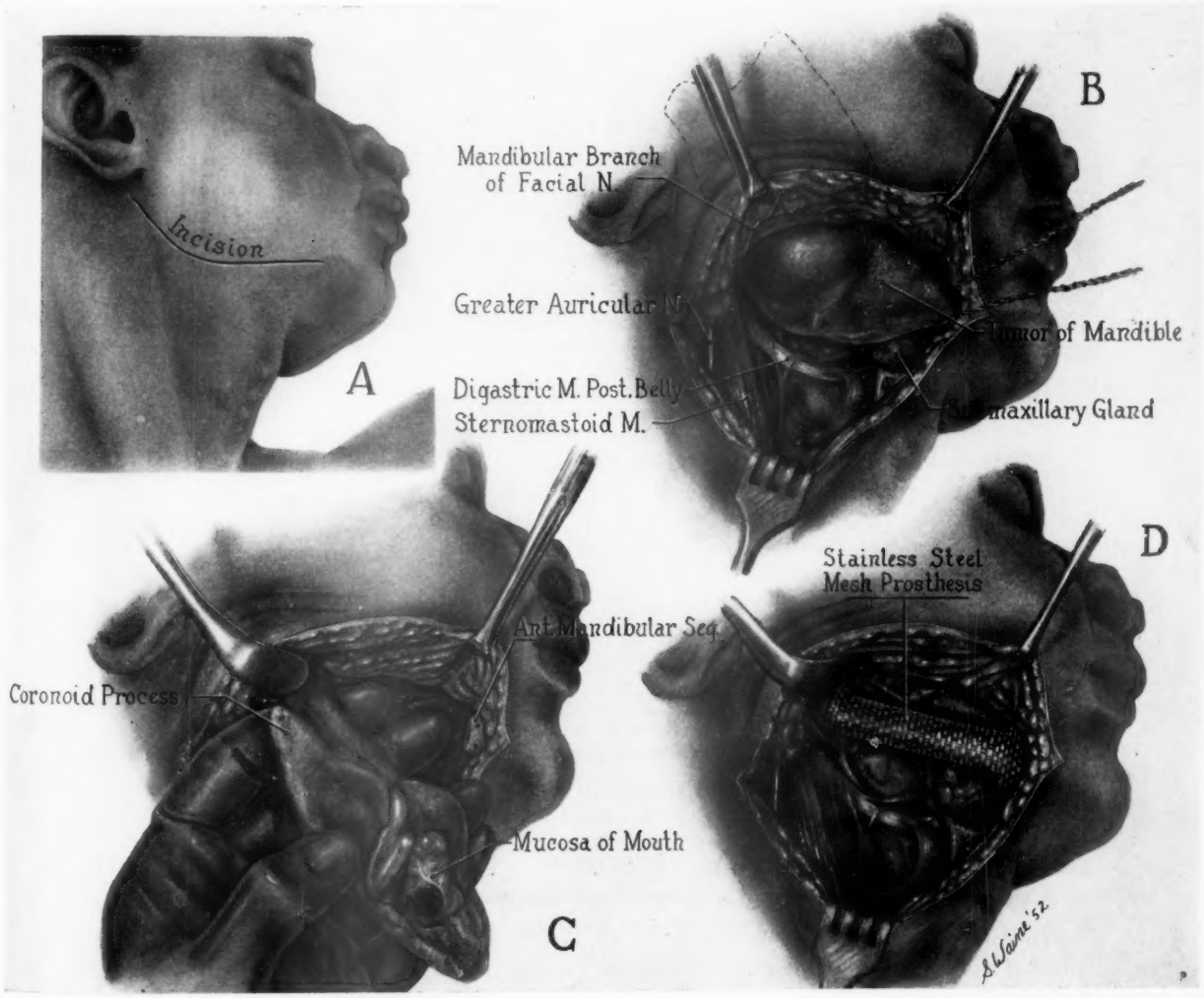

Fig. 5.—Operative approach.

A, A curved incision is made from the mastoid process, below the angle of the mandible, forward nearly to the midline.

B, The mandibular branch of the facial nerve is preserved. The periosteum is incised and reflected from the bone.

C, After two drill holes have been made in the mandible, the bone is divided with the Gigli saw and reflected downward and outward. The mandible is disarticulated and the specimen removed.

D, The stainless steel mesh prosthesis is insertedinto the defect and wired to the mandible anteriorly. The periosteum is surtured over the implant and the wound is closed.

usual advanced or recurrent case, segmental or total resection of the mandible is required.[3, 13] In contrast to most mandibular tumors, ameloblastoma often involves the ascending ramus and even the condyle.

Surgical Approach.—It was apparent from clinical and roentgenologic studies that the tumor in our patient involved the major portion of the right mandible, extending from the region of the second premolar to the base of the condyle. Although hemisection of the mandible has been performed entirely intraorally,[4] the poor exposure obtained and the increased danger of hemorrhage make this approach inadvisable. The most satisfactory approach is through a modified Kocher incision, starting at the mastoid process, passing downward and forward below the angle of the mandible, and upward and

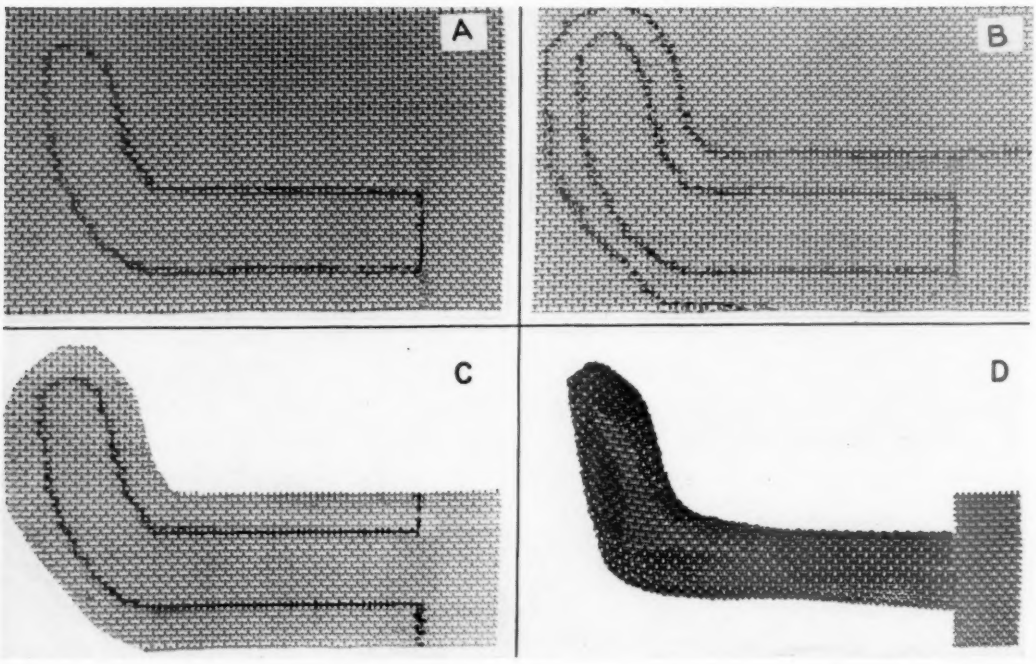

Fig. 6.—Preparation of prosthesis. Heavy stainless steel mesh (No. 20M) is used.
A, A draining of the projected prosthesis in actual size is traced on the steel mesh.
B, The tracing is enlarged 1.0 cm. on all sides to allow for infolding, and 1.5 cm. anteriorly for attachment to the mandible.
C, The mesh is cut with heavy scissors.
D, The edges are infolded with pliers, except for the anterior 1.5 cm.

forward nearly to the midline (Fig. 5, *A*). Care must be taken to identify and preserve the mandibular branch of the facial nerve. The periosteum is incised and reflected from the bone up to the level of the temporomandibular joint (Fig. 5, *B*). The exact anterior extent of the tumor is determined, and teeth lying in the line of resection are extracted. Before dividing the bone, two drill holes are made about 0.5 cm. anterior to the projected level of resection. The bone is divided with the Gigli saw and reflected laterally and downward (Fig. 5, *C*). The inferior dental vessels and nerve are visualized and ligated before division. The attachments of the coronoid process are cut and the mandible is easily disarticulated by gentle rocking. (Although a frag-

ment of mucosa was resected with the jaw in the case of our patient, it was not necessary to split the lip.) The mucosa is incised and later sutured through the mouth. The oral sutures must be placed with great care, using everting mattress sutures, to avoid fistula formation.

Preparation of Prosthesis.—Heavy stainless steel mesh (No. 20M)* was used. Based on clinical measurements and roentgenologic studies, a drawing of the projected prosthesis in actual size was traced on the steel mesh (Fig. 6, *A*). The tracing was then enlarged 1 cm. on all sides to allow for folding of the mesh, and 1.5 cm. anteriorly for attachment to the mandible (Fig. 6, *B*). The mesh was cut with heavy scissors and, except for the anterior 1.5 cm., the edges were infolded with pliers (Fig. 6, *C* and *D*). Care was taken to reproduce the angle accurately. The vertical portion was constructed shorter than the normal mandible with no attempt to replace the condyle. The completed prosthesis, prepared in a few minutes immediately prior to operation, was relatively light, inexpensive, and readily autoclaved. With the edges folded over, it was rigid and strong.

After removal of the specimen, the prosthesis was placed into the defect, and was fixed anteriorly to the mandible by two wire ligatures passed through the open portion of the mesh and the drill holes in the mandibular fragment (Fig. 5, *D*). The periosteum was sutured over the implant and the wound was closed.

Postoperative Care.—To prevent deviation of the mandible and to maintain normal occlusion, the jaws were wired for a period of ten weeks, at the end of which time active motion of the jaws was gradually resumed. During the immediate postoperative period, feedings were administered through a nasal catheter. The oral cavity was irrigated several times daily with 50 per cent hydrogen peroxide followed by normal saline until the mucosal suture line was healed. Penicillin was given for one week after operation.

SUMMARY AND CONCLUSIONS

1. A case of ameloblastoma of the mandible in a 13-year-old boy, with resection of nearly one-half of the mandible, including the condyle, is presented.
2. Various methods of mandibular replacement are briefly reviewed.
3. A new prosthesis designed from heavy stainless steel mesh is described. It has the advantages of being light, inexpensive, and rigid, and is constructed in a few minutes.

ADDENDUM

The patient was last examined on Dec. 7, 1952. At that time the prosthesis was firmly fixed to the remainder of the mandible and the cosmetic appearance was excellent. X-ray examination revealed some calcification occurring within the steel mesh. The patient was able to open and close the mouth without difficulty and there was a minimal degree of deviation of the mandible to the right when the mouth was fully opened.

REFERENCES

1. Byars, Louis T.: Subperiosteal Mandibular Resection With Internal Bar Fixation, Plast. & Reconstruct. Surg. 1: 236-239, 1946.

*"Foundation Wire Mesh" produced from 18-8-SMO stainless steel by United Surgical Company, New York, N. Y.

2. Byars, Louis T.: Preservation and Restoration of Mandibular Function and Contour, Ann. Surg. **127**: 863-878, 1948.
3. Catlin, Daniel: Adamantinoma of the Mandible, Ann. Surg. **129**: 505-511, 1949.
4. Castigliano, S. Gordon, and Gross, P. Philip: Immediate Prosthesis Following Radical Resection in Advanced Primary Malignant Neoplasm of the Mandible, J. Oral Surg. **9**: 31-38, 1951.
5. Conley, John J.: The Use of Vitallium Prostheses and Implants in the Reconstruction of the Mandibular Arch, Plast. & Reconstruct. Surg. **8**: 150-162, 1951.
6. Conway, Herbert: Reconstructive Surgery Following Radical Operations for Malignant Tumors of the Head and Neck, Ann. Surg. **131**: 64-79, 1950.
7. Freeman, Bromley S.: The Use of Vitallium Plates to Maintain Function Following Resection of the Mandible, Plast. & Reconstruct. Surg. **3**: 73-78, 1948.
8. Kleitsch, William P.: Vitallium Reconstruction of Hemi-Mandible and Temporo-Mandibular Joint, Plast. & Reconstruct. Surg. **7**: 244-253, 1951.
9. Lubschitz, Karen: Adamantinomas of the Jaw, With Special Reference to Their Treatment, Acta radiol. **26**: 441-455, 1945.
10. Marino, Hector, Turco, Nestor B., and Craviotto, Mario: Immediate Reconstruction of Lower Jaw Following Surgical Excision of Large Tumors, Plast. & Reconstruct. Surg. **4**: 36-44, 1949.
11. New, Gordon B., and Erich, John B.: Bone Grafts to Mandible, Am. J. Surg. **63**: 153, 1944.
12. Robinson, Hamilton B. G.: Ameloblastoma, A Survey of 379 Cases From the Literature, Arch. Path. **23**: 831-843, 1937.
13. Slaughter, Danely, Roeser, Erwin H., and Smejkal, Walter F.: Excision of the Mandible for Neoplastic Disease, SURGERY **26**: 507-523, 1949.
14. Venable, Charles S., and Stuck, Walter G.: A General Consideration of Metals for Buried Appliances in Surgery, Surg., Gynec. & Obst. **76**: 297-304, 1943.
15. Ward, Grant E., Williamson, Riley S., and Robben, John O.: The Use of Removable Acrylic Prosthesis to Retain Mandibular Fragments and Adjacent Soft Tissues in Normal Position After Surgical Resection, Plast. & Reconstruct. Surg. **4**: 537-544, 1949.
16. Winter, Leo, Lifton, Jacob C., and McQuillan, Arthur S.: Embedment of a Vitallium Mandibular Prosthesis as an Integral Part of the Operation for Removal of an Adamantinoma, Am. J. Surg. **69**: 318-324, 1945.

STUDIES IN THE UTILIZATION OF FRUCTOSE ADMINISTERED INTRAVENOUSLY IN MAN

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IT HAS recently been stated that invert sugar and fructose when given intravenously are retained and utilized to a greater extent by man than are equal quantities of glucose.[4, 8, 13, 15-19] In contrast to these reports, we found a greater quantity of reducing sugar in the urine of patients receiving one liter infusions of 10 per cent invert sugar than in that of those receiving equal quantities of 10 per cent glucose.[10] Because any difference in retention should depend upon the utilization of the fructose fraction of invert sugar, additional studies were conducted. This paper is a report of the results obtained when equal amounts of fructose and glucose were given intravenously to men under similar circumstances.

METHODS

The patients studied were male adults in the surgical wards of the Wadsworth Hospital, Veterans Administration Center, Los Angeles. The age of the patients ranged from 29 to 69 years. They did not have debilitating diseases and were not in the immediate postoperative period. For the purposes of this study, two groups of experiments were conducted.

Group One.—The eleven patients in this group were placed in a fasting state for nine hours. At the end of this time a blood sample was drawn for the determination of sodium, potassium glucose, and fructose levels. The patients voided and a twenty-four hour urine collection was begun. The patients were then allowed a standard hospital diet with unrestricted fluid intake until midnight of the same day. At midnight the patients were again placed in a fasting state for nine hours. The twenty-four hour urine collection was terminated and was assayed for volume, specific gravity, total glucose, total fructose, sodium, potassium, and chloride. A second twenty-four hour urine collection was then begun. A fasting blood sample was drawn for the purpose of obtaining the same determinations as on the preceding day. An intravenous infusion was then started. Four patients received 1,000 c.c. of 10 per cent fructose and the other seven patients received 1,000 c.c. of 10 per cent glucose. Both solutions were in distilled water. The period of infusion varied from two and one-half to three and one-half hours. Blood samples for the determination of the glucose and fructose levels were drawn at one-half hour,

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TABLE I. COMPARISON OF EXCRETION OF SOLUTES AFTER SINGLE INTRAVENOUS INFUSION OF GLUCOSE AND FRUCTOSE

	1 L. 10% GLUCOSE IN H_2O						1 L. 10% FRUCTOSE IN H_2O				
		24 HOUR URINARY EXCRETION						24 HOUR URINARY EXCRETION			
PATIENT	GLUCOSE INTAKE (GM.)	VOL. URINE (C.C.)	SUGAR (GM.)	SODIUM (MEQ.)	POTASSIUM (MEQ.)	PATIENT	SUGAR INTAKE (GM.)	VOL. URINE (C.C.)	SUGAR (GM.)	SODIUM (MEQ.)	POTASSIUM (MEQ.)
					Control Period						
Po.	diet	1,200	1.20	159	62	Cr.	diet	1,663	1.61	156	49
Hu.	diet	3,100	2.17	142	61	Do.	diet	1,842	1.30	146	42
Mc.	diet	1,200	1.56	167	70	Ta.	diet	1,938	0.496	153	46.8
Ke.	diet	1,550	1.86	181	80	Ca.	diet	1,726	0.78	142.3	39.6
Jo.	diet	4,000	0.424	173	93						
Ma.	diet	1,150	0.83	164	80						
Ga.	diet	1,700	0.57	148	42						
Average		1,986	1.23	162	69			1,792	1.06	149.2	44.35
					Infusion Period (24 Hour Collection)						
Po.	100	2,900	3.19	150	56	Cr.	100	1,560	4.435	464	113.0
Hu.	100	3,800	4.59	130	79	Do.	100	1,390	9.056	280	73
Mc.	100	1,800	2.49	156	76	Ta.	100	1,900	6.158	532	108.8
Ke.	100	1,600	2.30	158	84	Ca.	100	3,130	6.617	481	163.8
Jo.	100	3,600	3.99	169	91						
Ma.	100	1,200	1.68	152	97						
Ga.	100	1,565	6.734	132	27.7						
Average		2,352	3.57	149	73			1,995	6.566	439	114.6

one hour, two hours, and three hours following the beginning of the infusions. Urine collections were made at two, four, six, eight, and twenty-four hour intervals after the start of the infusion. Each urine sample was assayed for volume, specific gravity, glucose, fructose, sodium, potassium, and chloride content. The patients received no oral or parenteral intake other than the single infusion during the twenty-four hour study and measured amounts of distilled water, not exceeding 500 c.c., by mouth.

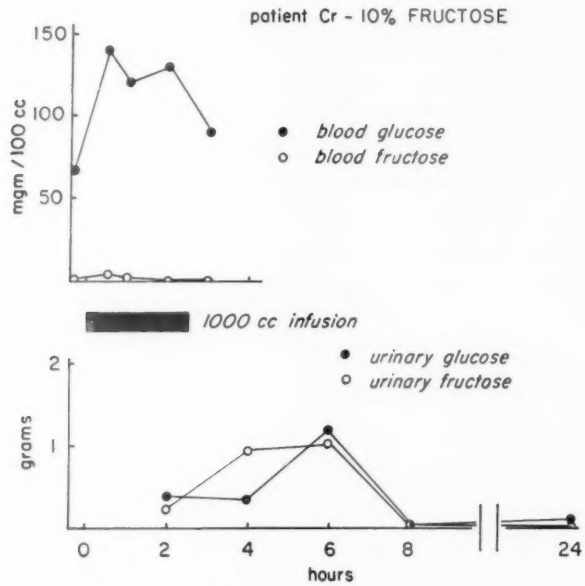

Fig. 1.—Graphic representation of blood sugar levels and urinary sugar excretion in male adult (Cr.) weighing 64 kilograms. He received single intravenous infusion of 1 L. of 10 per cent fructose, over a 2.5 hour period. Approximate rate of injection was 0.62 Gm. of fructose per kilogram per hour.

Group Two.—Eight patients comprised the second group. A twenty-four hour control period was obtained as in the preceding group. Oral intake was then withheld for approximately nine hours after midnight. The twenty-four hour urine collection from the preceding day was closed and a fasting blood sample was drawn. Urine collection was begun and an infusion was started. During the next five days four patients were given 3,000 c.c. of 10 per cent fructose (300 Gm.) intravenously during each twenty-four hour period. Electrolytes were given intravenously by means of 500 c.c. of 0.9 per cent saline solution to which was added from 20 to 60 meq. of potassium as potassium chloride. Measured amounts of distilled water not exceeding 500 c.c. were allowed by mouth each day. Urine was collected every two hours for eight hours after the initiation of the infusion, and a final sixteen hour collection completed the twenty-four hour urine collection. Blood samples were obtained at one-half, one, two, and three hours after the beginning of the infusion. Analyses of the blood and urine specimens were made, as in the preceding study.

Total reducing sugar in the urine was measured by the method of Somogyi,[11] and urinary sodium and potassium were determined on a Weichselbaum-

Varney flame photometer.[14] Determinations of blood and urinary fructose were made by the method of Higashi and Peters,[5] modified for the Beckman spectrophotometer with readings made at 620 mμ. Blood reducing sugar was determined by the method of Somogyi.[7] Serum sodium and potassium values were obtained by the method of Weichselbaum and Varney.[14] Blood and urinary chlorides were determined by the method of Kingsley and Dowdell.[6]

RESULTS

Group One.—The results of these studies are summarized in Table I. It may be seen that the patients receiving 1 L. of infusions of 10 per cent glucose excreted from 1.68 to 6.734 Gm. of reducing sugar during the twenty-four hour period of study, with an average of 3.57 Gm. for the six patients investigated. The patients receiving equal amounts of 10 per cent fructose excreted from 4.435 to 9.056 Gm. of reducing sugar during the twenty-four hour period, with an average excretion of 6.566 Gm. The twenty-four hour excretion of fructose in this latter group varied from 2.256 to 3.518 Gm.

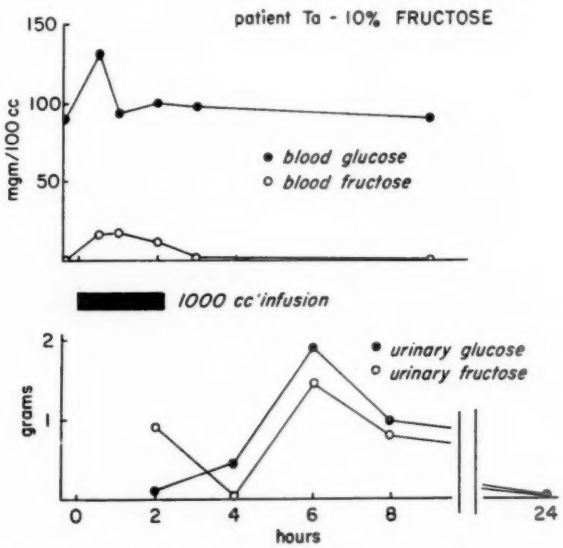

Fig. 2.—Blood sugar levels and urinary excretion in patient (Ta.) who received 1 L. of 10 per cent fructose intravenously over a 2.2 hour period. The approximate rate of injection was 0.56 Gm. of fructose per kilogram per hour.

Examination of the pattern of urinary excretion in the patients receiving fructose (Figs. 1 and 2) demonstrated that the maximum excretion occurred in the specimen obtained for the two-hour period ending six hours from the start of the infusion. This was approximately four hours after completion of the infusion. An elevation of both blood glucose and blood fructose occurred during the infusion, but the maximum urinary excretion did not occur until one and one-half to two hours after the blood levels had returned to normal. The maximum blood glucose level was 153 mg. per 100 c.c., and the maximum blood fructose level was 19.96 mg. per 100 c.c. in the four patients receiving intravenous fructose.

It may be seen in Fig. 3 that the intravenous injection of 10 per cent glucose results in a slightly different pattern of urinary excretion. The appearance of an increased amount of glucose in the urine occurs somewhat sooner than with fructose, and the excretion curve follows a more prolonged and gentle slope. The blood levels of reducing sugar did not differ materially from those obtained with intravenous fructose.

In Table I it may also be noted that the patients who were given 1 L. injections of 10 per cent fructose excreted considerably greater quantities of sodium and potassium during the period of observation than did the group receiving glucose. The amount of excretion does not seem to be related to the volume of urine.

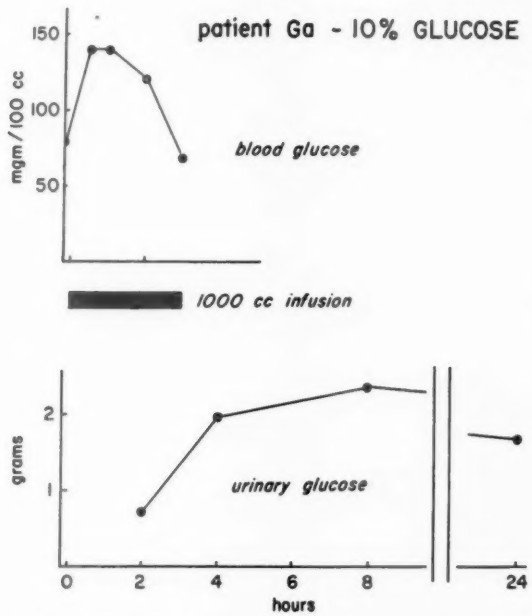

Fig. 3.—Graph showing blood and urinary sugar analyses after a single 1 L. intravenous injection of 10 per cent glucose over a 3 hour period. Approximate rate of injection was 0.46 Gm. kilogram per hour.

Group Two.—The results of these studies are presented in Tables II and III. Although there was considerable variation in the total quantity of reducing sugar present in the twenty-four hour urine collections, the excretion of total reducing sugar in the urine of the patients receiving 300 Gm. of fructose intravenously daily was consistently greater than in those who were given 300 Gm. of glucose. In those to whom fructose was administered, the urinary reducing sugar included significant quantities of fructose. The excretion of electrolytes was also greater in those receiving intravenous fructose. The loss of sodium probably accounts for the greater average loss of weight in this group.

Figs. 4 and 5 represent graphically the urinary loss of reducing substances in one patient during two twenty-four hour collections. It may be seen that although the rate of injection varied, the excretion of fructose followed the

TABLE II. STUDIES ON PATIENTS RECEIVING 3 LITERS OF 10 PER CENT GLUCOSE DAILY (300 GM. GLUCOSE)

PATIENT	SEX	AGE (YEARS)	DAYS STUDIED	AVERAGE DAILY INTAKE			AVERAGE DAILY URINARY EXCRETION			
				VOL. (C.C.)	SODIUM (MEQ.)	POTASSIUM (MEQ.)	VOL. (C.C.)	TOTAL REDUCING SUGAR (GM.)	SODIUM (MEQ.)	POTASSIUM (MEQ.)
Th.	M	29	5	3,836	77	73	3,776	13.163	115	54.6
Br.	M	58	5	3,780	77	120	3,405	13.70	77	35.99
Mc.	M	69	5	3,757	77	120	3,280	16.29	88	28.1
Ro.	M	33	3	3,845	77	60	3,395	5.006	166	90.3

TABLE III. STUDIES ON PATIENTS RECEIVING 3 LITERS OF 10 PER CENT FRUCTOSE DAILY (300 GM. FRUCTOSE)

PATIENT	SEX	AGE (YEARS)	DAYS STUDIED	AVERAGE DAILY INTAKE			AVERAGE DAILY URINARY EXCRETION			
				VOL. (C.C.)	SODIUM (MEQ.)	POTASSIUM (MEQ.)	VOL. (C.C.)	TOTAL REDUCING SUGAR (GM.)	SODIUM (MEQ.)	POTASSIUM (MEQ.)
Sp.	M	56	5	3,644	46	40	3,479	30.305	284	122
Gu.	M	52	5	3,613	46	40	3,341	20.364	223	84
Sp.	M	56	5	3,611	62	56	3,222	23.887	182	36
Bo.	M	59	4	3,444	58	42	3,098	29.691	190	66

same pattern, with a sharp peak in the two-hour sample obtained six hours after the start of the infusion and another in the sixteen-hour specimen obtained at twenty-four hours. The excretion of the glucose fraction was influenced by the variation in the rate of injection, and a larger quantity appeared in the last specimen when the injection was given more rapidly. The blood levels were apparently little influenced by the rate of injection used.

Fig. 6 contrasts the pattern of excretion obtained when a quantity of glucose equal to the amount of fructose given to the patient in Fig. 4 was given over a period of time comparable to the one employed in the case of the previous patient. In the patient given glucose, the excretion increased more slowly and then gradually fell. The level of blood reducing sugar reached a higher level but returned to normal in approximately the same length of time as it did in the patients who received fructose, although the infusion of glucose continued.

DISCUSSION

The results of the investigations in this paper and those in our previous studies[10] fail to substantiate the reports that invert sugar and fructose are better utilized by human beings than is glucose when given intravenously. Not only did greater quantities of reducing substances appear in the urine of patients receiving fructose solutions by vein, but, in addition, a diuretic effect was indicated by a significantly greater excretion of electrolytes.

While we cannot entirely account for the differences in our results when compared with those reported elsewhere, the following factors may have some bearing on this aspect. In some of the published reports, collection of urine was terminated three hours after the end of the infusion period.[13, 19] In our studies it was noted that the maximum excretion of reducing sugar appeared

in the two-hour urine sample collected six hours after the start of the infusion, or slightly more than three hours after the completion of the injection. Also, significant quantities of reducing sugars were often still present in the urine in the subsequent two-hour specimen. The disparity in retention was much more marked in the five-day studies when the patients were given 3 L. injections of 10 per cent fructose and 10 per cent glucose.

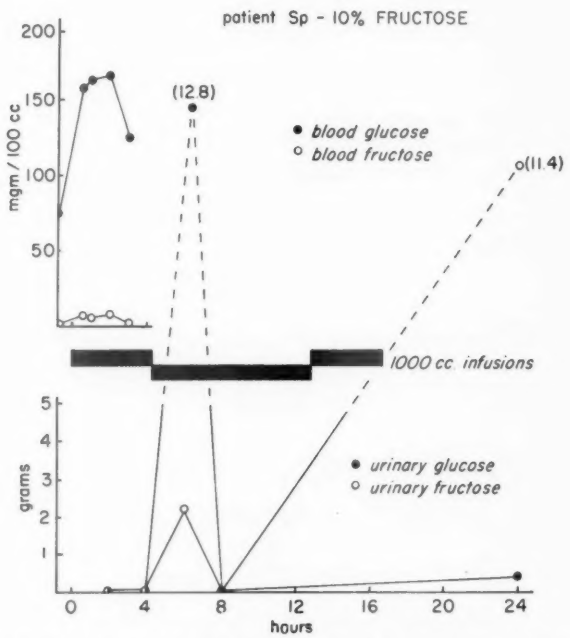

Fig. 4.—Graphic presentation of blood and urinary sugar determinations in patient (Sp.) who received 300 Gm. of fructose at an average rate of 0.34 Gm. per kilogram per hour.

In these studies, rapid rates of injection such as have been described by Weinstein were not employed. It appears undesirable to us to stress rapidity of injection in administering intravenous fluids, because of possible embarrassment to the circulation. Utilization of both invert sugar and glucose is better with longer periods of injection. However, speed may be a factor in interpreting utilization of fructose and glucose with 1 L. infusions when both are given at rates exceeding the tolerance. Cori and Cori,[2] in experiments on rats, found that when glucose or fructose was infused at a rate far above the tolerance limit, there was no marked difference in the rate of utilization of these two sugars. They had found the tolerance rate for fasting rats to be 0.35 Gm. per kilogram per hour for fructose, as compared with 2.5 Gm. per kilogram per hour for glucose.

The methods of analysis may also have influenced our findings. Most of the recent reports on the efficacy of invert sugar and fructose have employed a Folin-Wu method of determining total glucose excretion.[15-19] In our investigations the Somogyi method was used to determine total reducing substances more accurately. That this may be of some importance is suggested by

the finding of Bodansky,[1] who stated that following the ingestion of fructose or galactose, the urine contains reducing substances other than these monosaccharides.

Because there has been some controversy concerning the manner in which fructose is utilized by the human being, some observations seem worth mentioning. It has been stated that the rise in blood sugar is much less after the administration of fructose than after the injection of a similar quantity of glucose.[3] In our studies, the blood sugar level tended to rise to a slightly higher level in the group receiving intravenous injections of glucose; however, in some patients who received glucose the blood sugar levels were no higher than in some of those given fructose.

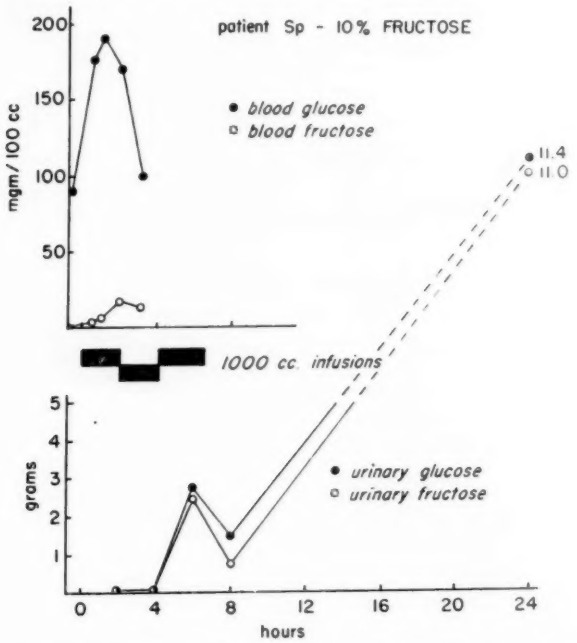

Fig. 5.—This chart was obtained from the same patient shown in Fig. 4 (Sp.) on following day. Injection was made at an approximate average rate of 0.7 Gm. per kilogram per hour.

In 1915 Woodyatt, Sansum, and Wilder[20] reported that glycosuria did not appear until the rate of injection of glucose was faster than approximately 0.85 Gm. per kilogram per hour. These investigators also found that the tolerance limit for fructose by intravenous injection was approximately 0.15 Gm. per kilogram per hour. The patients receiving repeated infusions of fructose (300 Gm. per twenty-four hours) were given injections varying from 0.3 to 0.7 Gm. of fructose per kilogram per hour, which was greater than the tolerance rate determined by Woodyatt and his associates. In each case melituria occurred. These findings are in conflict with those of Weinstein,[19] who reported that the tolerance for invert sugar is 1.5 Gm. per kilogram per hour. Because urine collections were made at two-hour rather than at one-hour intervals, it was difficult to determine accurately the tolerance limit for glucose. However, it would appear on the basis of these studies to be somewhat lower

than that stated by Woodyatt. In the patients who received 300 Gm. of glucose in approximately eight hours, the tolerance limit appeared to be in the neighborhood of 0.6 Gm. per kilogram per hour. This more nearly approaches the figure quoted by Lockhart and Elman.[9]

Because of the low renal threshold for fructose, it does not seem surprising that fructose should be retained to a lesser extent than glucose when given intravenously. Deuel[3] has stated that if there is a renal threshold for fructose it must be extremely low, because definite quantities of fructose appear in the urine after moderate amounts are taken, even though the blood fructose level remains low. Although fructose appears to be a more efficient glycogen-former than glucose, it does not appear to be transformed into glycogen or glucose with sufficient rapidity when given intravenously to escape from the circulation and thus be inaccessible to the kidney for excretion.

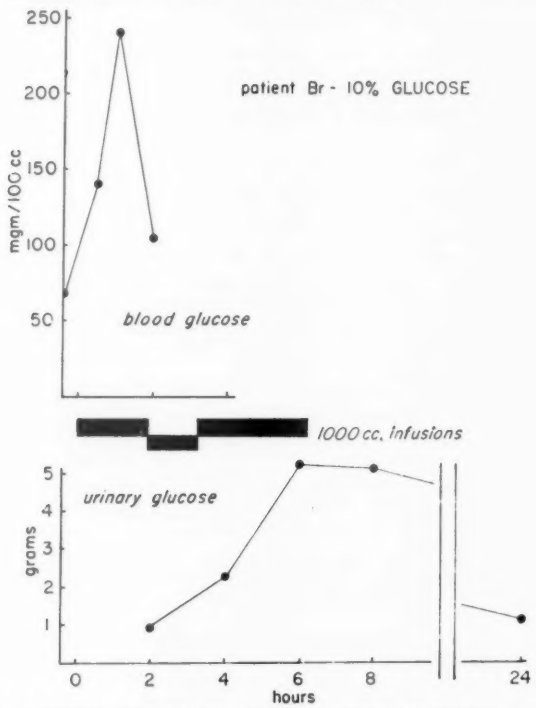

Fig. 6.—Graph showing urinary and blood determinations in patient (Br.) who received 300 Gm. of glucose at a rate of 0.65 Gm. per kilogram per hour.

The association of an increased electrolyte loss with a lower retention indicates that fructose is not a suitable substitute for glucose in parenteral alimentation in human beings.

SUMMARY

Under the conditions of these experiments, 10 per cent fructose when injected intravenously was not retained in men as well as was 10 per cent glucose, whether given in single 1 L. infusions or in 3 L. infusions for several days.

The intravenous administration of 10 per cent fructose was associated with a definite increase in electrolyte excretion as compared to injection of similar quantities of 10 per cent glucose.

REFERENCES

1. Bodansky, M.: Fructose, Glucose, and Galactose Tolerance in Dogs, J. Biol. Chem. **56**: 387, 1923.
2. Cori, G. T., and Cori, C. F.: The Fate of Sugar in the Animal Body: IV. The Tolerance of Normal and Insulinized Rats for Intravenously Injected Glucose and Fructose, J. Biol. Chem. **72**: 597, 1927.
3. Deuel, H. J.: The Intermediate Metabolism of Fructose and Galactose, Physiol. Rev. **16**: 173, 1936.
4. Frost, D. V., Miller, J. P., and Richards, R. K.: Some Considerations Regarding Invert Sugar and Dextrose, J. Appl. Physiol. **4**: 793, 1952.
5. Higashi, A., and Peters, L.: A Rapid Colorimetric Method for the Determination of Inulin in Plasma and Urine, J. Lab. & Clin. Med. **35**: 475, 1950.
6. Kinsley, G. R., and Dowdell, L. A.: Direct Iodometric Determination of Blood Chloride, J. Lab. & Clin. Med. **35**: 637, 1950.
7. Koch, F. C., and Hanke, M. E.: The Shaffer-Hartman-Somogyi Method for the Determination of Reducing Sugars in Blood. Practical Methods in Biochemistry, ed. 5, Baltimore, 1948, Williams and Wilkins Company, p. 204.
8. Lawton, B. R., Curreri, A. R., and Gale, J. W.: Use of Invert Sugar Solutions for Parenteral Feeding of Surgical Patients, Arch. Surg. **63**: 561, 1951.
9. Lockhart, C. E., and Elman, R.: Effect of Intravenous Glucose and Amino Acids on Glycosuria and Urinary Output in Humans, Surg., Gynec. & Obst. **88**: 97, 1949.
10. Smith, J. L., Beal, J. M., and Frost, P.: Comparative Utilization of Intravenous Invert Sugar and Glucose, SURGERY **31**: 720, 1951.
11. Somogyi, M. A.: Rapid Method for the Estimation of Urine Sugar, J. Lab. & Clin. Med. **26**: 1220, 1941.
12. Strub, I., Best, W. R., Marek, E., and Grossman, M. I.: Blood and Urinary Sugar Levels After Intravenous Infusion of Glucose, Fructose, and Invert Sugar in Human Subjects, Fed. Proc. **11**: 156, 1952.
13. Weichselbaum, T. E., Elman, R., and Lund, R. H.: Comparative Study of Glucose and Fructose Given Intravenously, Proc. Soc. Exper. Biol. & Med. **75**: 816, 1950.
14. Weichselbaum, T. E., and Varney, P. C.: Manual of Operation and Maintenance for the Weichselbaum-Varney Flame Spectrophotometer Manual VS-No. 120, The Fearless Camera Co., Los Angeles.
15. Weinstein, J. J.: Intravenous Infusions of Invert Sugar; a Preliminary Report, M. Ann. District of Columbia **19**: 179, 1950.
16. Weinstein, J. J.: Parenteral Therapy With Invert Sugar, Ann. West. Med. & Surg. **4**: 373, 1950.
17. Weinstein, J. J., and Lane, G. F.: Rapid Infusions of Invert Sugar, M. Ann. District of Columbia **20**: 186, 1951.
18. Weinstein, J. J.: Comparative Utilization of Invert Sugar and Dextrose in Nondiabetic Human Beings, M. Ann. District of Columbia **20**: 355, 1951.
19. Weinstein, J. J.: Tolerance of Human Beings to Intravenous Infusions of Fifteen Per Cent Invert Sugar, J. Lab. & Clin. Med. **38**: 1, 1951.
20. Woodyatt, R. T., Sansum, W. D., and Wilder, R. M.: Prolonged and Accurately Timed Intravenous Injections of Sugar; a Preliminary Report, J. A. M. A. **65**: 2067, 1915.

CLINICAL EXPERIENCES IN THE USE OF N-ALLYLNORMORPHINE (NALLINE) AS AN ANTAGONIST TO MORPHINE AND OTHER NARCOTICS IN SURGICAL PATIENTS

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ALTHOUGH many new drugs and methods for relieving pain in surgical patients have been recently introduced, the opium alkaloids and their synthetic substitutes are still relied upon for this purpose. Respiratory and circulatory depression from overdosage or intolerance to these substances are not uncommon and frequently cause concern. Heretofore, there has been no satisfactory treatment for the depression from overdosage of morphine and its allies. The management has, to a large extent, been symptomatic and supportive. The analeptic drugs ordinarily used for depression from morphine, such as atropine, caffeine, Metrazol, or nikethamide, are not specific and the responses, if any, are transient. There is a need for a better antagonist or specific antidote. Recently a morphine derivative has been prepared which offers promise of being a specific antidote for overdosage due to narcotics. This compound is N-allylnormorphine. It differs from morphine in having the methyl group on the nitrogen atom replaced by an allyl group. Unna,[1] in 1943, observed that the compound antagonized most of the actions of morphine in animals. Hart and McCawley,[2] in 1944, confirmed these results. Later Huggins and Glass[3] and Smith, Lehman, and Gillfillan[4] noted that N-allylnormorphine overcame the respiratory depression caused by Demerol Hydrochloride and methadone hydrochloride. These narcotics are pharmacologically similar but chemically different from morphine. In rats, N-allylnormorphine appears to have an analgesic effect, but is not nearly as potent as morphine in this respect. However, this does not appear to be true in dogs. Premedication of rats and dogs with this substance increased the resistance to morphine so that lethal doses were tolerated without the usual respiratory and circulatory depression.

The drug is derived from morphine. It is, therefore, placed under the scope of the Harrison Narcotic Act and is not available without prescription. There is sufficient evidence to indicate that it is nonaddicting and will not relieve the withdrawal symptoms of morphine abstinence in addicts. Recently, Merck & Co., Inc., Rahway, N. J., has packaged the material in sterile ampules for parenteral use under the proprietary name of Nalline. Each ampule contains 10 mg. in 5 mg. per cubic centimeter concentration in the form of the hydrochloride salt. The solution is colorless and appears to be stable in sealed ampules. The solutions used for investigational purposes, packaged in rubber-stoppered bottles, turned yellow after several months, indicating oxidation. The

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preparation in sealed glass ampules appears to be more stable. When the ampules are opened, the drug quickly deteriorates and forms a brown solution. Discoloration indicates decomposition, and the drug is probably not effective. Two clinical reports are available concerning its use in man.[5, 6] This is a report of its use in over forty-eight surgical patients in whom overdosage or intolerance to morphine and its substitutes had actually occurred or were suspected.

The most common symptom of overdosage from morphine and other opium alkaloids in man is depression of respiration. The respiratory depression from morphine is characterized by a marked decrease in rate but an increased tidal volume. In eleven patients who received an excess of morphine, respiratory depression was the predominant symptom. The following three case reports illustrate the usefulness of the drug for overcoming depression of respiration.

CASE 1.—A 76-year-old white man underwent surgery for a gastrectomy, which was performed using cyclopropane-ether anesthesia. One hour before induction of anesthesia was attempted, he was given ¼ gr. of morphine and 1/150 gr. of atropine subcutaneously. He was breathing deeply 4 times per minute at time of surgery. The exchange was not adequate and attempts to induce surgical anesthesia were futile. Ten milligrams of N-allylnormorphine were administered slowly intraveneously. The respiratory rate rose to 12 per minute. Ether anesthesia was then induced with ease. Respirations rose to 24 where they remained during the next four hours until the operation was completed.

CASE 2.—M. C., a 29-year-old white woman, underwent surgery for a fenestration operation of the right ear. Thirty minutes before anesthesia she received hypodermically ¼ gr. of morphine, and 1/150 gr. of atropine. Induction of anesthesia using cyclopropane was attempted but the respiratory exchange was so inadequate (6 per minute) that the use of cyclopropane was abandoned. Induction and intubation were continued, instead, with nitrous oxide and ether, the respiration stabilizing between 16 to 20 per minute. After intubation, anesthesia was maintained with nitrous oxide, oxygen, and basal of pentothal, because an electric drill was to be used. One hundred milligrams of pentothal was given. This was administered approximately one and one-half hours after the premedication. Respirations again dropped to 6 within the next half hour. The patient was at no time cyanotic. At that time 2.5 mg. of N-allylnormorphine was administered intravenously. Within two minutes respirations rose to 20 per minute and remained at that level. The operation and postoperative course were uneventful.

CASE 3.—A. S., a 63-year-old white woman, presented a history of chronic alcoholism. She was icteric for five days prior to admission and had had abdominal pain for three days. She was given a "hypo" (thought to be 1/6 gr. of morphine and 1/150 gr. of atropine) at 2:00 P.M. by her private physician at home so that he could examine her. She slowly lapsed into a coma and then was admitted to Charity Hospital. When the patient was seen at 11:30 P.M. the respirations were 8 per minute, the pupils were pin point, and she was in a deep coma. Ten milligrams of N-allylnormorphine was given intravenously. Within thirty seconds respirations rose to 24 and the pupils became partly dilated; the patient stirred about and responded to stimulation. The respiratory rate remained above 20 per minute for six hours and then dropped to 14. Ten milligrams of N-allylnormorphine was again administered intravenously at 7:00 P.M. The respiratory rate rose to 24 and did not decrease until the patient died two days later from acute liver failure and bronchopneumonia.

The drug worked as effectively in the remaining eight cases.

In present-day surgical practice combinations of hypnotics, particularly the barbiturates and narcotics, are widely used. Respiratory depression often develops in the preoperative or postoperative period. It is frequently difficult

to determine which of the two is causing the depression in these situations. In some instances the narcotic alone is responsible; in others the effect is due to the barbiturate; and in still others it is due to the combined effect. The drug was used in six cases in which combinations had been used. The following cases illustrate the usefulness of the drug under such circumstances.

CASE 4.—G. H., a 48-year-old white woman, underwent surgery for bilateral cataracts. Local anesthesia, combined with intravenous Seconal Sodium (250 mg.), Pentothal Sodium (1 Gm.), and curare (forty-five units), was employed. When the patient was returned to the recovery division the respiratory rate was 10 per minute. One and one-half hours later 100 mg. of Demerol Hydrochloride was administered subcutaneously for restlessness. Twenty minutes later respirations ceased entirely, necessitating the use of artificial respiration. N-allylnormorphine, 12.5 mg., was given intravenously. Respirations rose to 7 per minute and remained at this rate during the next four hours. At this time 3 mg. of picrotoxin was administered intravenously. The respiratory rate rose to 14 per minute and remained at this level. Obviously both the barbiturates and the narcotic contributed to the depression in this instance.

CASE 5.—L. S., a 24-year-old Negro woman, was admitted for toxemia of pregnancy. The blood pressure ranged between 180/126 to 240/150. After having received a total of 8 gr. of phenobarbital, the patient was given 0.25 gr. of morphine. Several hours later the same dose of the morphine was repeated. One and one-half hours later the respiration dropped from 18 to 8 per minute. She delivered spontaneously at 2:00 P.M. The blood pressure at that time was 220/130. The baby's respiration was depressed at first, but it breathed adequately after seven to eight minutes. The mother was given 20 mg. of N-allylnormorphine intravenously, slowly. By 2:30 P.M. the blood pressure was 140/50, pulse 72, and respiration 8. At 3:00 P.M. the blood pressure was 200/140, pulse 74, and respiration 12. At this time the patient roused and became excited and uncooperative. She remained somewhat excited for about thirty minutes. During the next five hours, respirations remained between 8 and 10 per minute and the blood pressure slowly fell to 140/100. By midnight, respiration had increased to 18 and remained at that level.

The response is not as dramatic when there are combinations of narcotics and barbiturates. In a half dozen instances in which barbiturates alone were the obvious cause of respiratory depression 10 mg. doses of N-allylnormorphine were totally without effect.

In four instances the N-allylnormorphine was used to overcome the depression of respiration in the newborn when morphine had been inadvertently administered to the mother just before delivery. The following case illustrates its effectiveness for this purpose.

CASE 6.—P. L., a Negro woman, was admitted at 2:00 A.M. with convulsions due to toxemia. Four grains of Amytal were administered over a thirty-minute period. She was considerably disoriented and uncooperative. At 4:00 A.M. her behavior was almost maniacal and she was given ¼ gr. of morphine and 3 gr. of phenobarbital intravenously. At 8:00 A.M. ¼ gr. of morphine and 3 gr. of phenobarbital were again repeated. At 11:30 A.M. ⅙ gr. of morphine and 3 gr. of phenobarbital were again given intravenously. At 3:55 P.M. the blood pressure was 130/90 and respiratory rate 18. Morphine, ⅙ gr., and atropine, $\frac{1}{150}$ gr., were again administered intravenously. A low cervical cesarean section was performed using local anesthesia (1 per cent procaine) at 5:10 P.M. Respiration of the newborn was severely depressed. He made occasional gasps two or three times per minute. An endotracheal

catheter was inserted and artificial respiration was instituted by insufflation of oxygen with a bag and mask. N-allylnormorphine, 2.5 mg., was administered in the umbilical vein. Within thirty seconds the respiratory rate was 20 to 25 per minute and remained at that level from then on. Within five minutes the infant coughed from reaction to the catheter, which was then removed.

It is not uncommon for patients heavily premedicated, particularly when combinations of narcotics and barbiturates are used, to undergo surgery with a hypotension. In five instances N-allylnormorphine has proved effective in restoring the blood pressure to its preanesthetic levels. In five instances it was ineffective. The following are two case reports illustrating its use for this purpose. In one it was effective; in the other it was not.

CASE 7.—B. P., a 77-year-old white man, underwent surgery for a suprapubic prostatectomy. Premedication of 75 mg. of Demerol Hydrochloride and 1/150 gr. of atropine were administered subcutaneously at 9:00 A.M. Spinal anesthesia was induced by using 12 mg. of Pontocaine Hydrochloride at 10:10 P.M. The anesthesia began to "wear off" before the end of the procedure. One-eighth grain of morphine and 50 mg. of Seconal Sodium were given intravenously at 11:50 P.M. The respiratory rate fell to 10 per minute, the pulse was 68 per minute, and blood pressure could not be obtained. Ten milligrams of N-allylnormorphine was administered intravenously over a five-minute period. At the conclusion of the injection the blood pressure was 140/80, pulse 84, and respiratory rate 10 per minute. Ten minutes later the blood pressure was 160/90, pulse 88, and respiratory rate 28 to 30 per minute, remaining at this level.

CASE 8.—C. B., a 50-year-old Negro man, was brought to surgery for a gastrectomy for a bleeding peptic ulcer. He was not bleeding at the time of operation and he had received multiple blood transfusions preoperatively. The preoperative blood pressure was 152/110. One-sixth grain of morphine and 1/150 gr. of atropine were administered subcutaneously at 9:30 A.M. At 10:00 A.M. preanesthetic blood pressure was 84 by palpation, pulse 112, respiration 12. A transfusion was started. The stomach contents were aspirated, but no blood was present. Five milligrams of N-allylnormorphine was given intravenously with no effect. The blood pressure continued to vary between 86 and 90 by palpitation. Ephedrine, 10 mg. intravenously, was without effect and the operation was deferred.

Obviously, a hypotension immediately preoperatively may be due to causes other than the premedication. In the instances in which the N-allylnormorphine failed to restore the blood pressure to the preanesthetic level, there was no aggravation of the circulatory depression.

In fifteen instances respiratory depression of undetermined origin occurred in the postoperative period. The morphine dosage was not excessive but was considered as a possible cause of the respiratory depression. In these instances the drug appeared to be ineffective. The following is a typical case.

CASE 9.—A 70-year-old Negro man was given 1/8 gr. of morphine, and 1/150 gr. of atropine, preoperatively. A gastrectomy was performed under ether anesthesia, lasting four hours. Approximately thirty minutes after the patient was returned to bed, it was noted that the respiratory rate was 6 per minute. The blood pressure was 110/70 and the pulse 80. Slight cyanosis was noted at nail beds. Five milligrams of N-allylnormorphine was administered intravenously. There was no effect on respiration. The blood pressure rose to 170/100. A second 5 mg. dose was then administered with no effect, and use of the drug was abandoned. The blood pressure remained elevated for twenty minutes.

In one instance the drug was used when nausea followed the use of morphine for preoperative medication. The retching and vomiting began after the administration of ¼ gr. of morphine for preanesthetic medication. It interfered with induction of anesthesia. Five milligrams of N-allylnormorphine were given intravenously. Within three minutes the retching ceased and the induction of anesthesia proceeded without event.

DISCUSSION

N-allylnormorphine appears to be the drug of choice for the treatment of overdosage of narcotics. It appears to be effective in doses of 5 to 10 mg., in most instances. It has the advantage of not causing convulsions in man, which is not the case with other analeptics, such as Metrazol, picrotoxin, or nikethamide. In the event it is ineffective in reversing the respiratory depression, it does not cause further depression as other analeptics frequently do. If the drug is given to patients who have respiratory depression due to causes other than the narcotic, it does not stimulate respiration. It is ineffective in reversing narcosis from ether or the barbiturates or in overcoming respiratory difficulties due to anoxia. A transient rise in blood pressure was noted in nine instances, but this was not of alarming proportions. Large doses of 30 or 40 mg. may cause depression and one is, therefore, cautioned in ordinary circumstances not to exceed 10 or 15 mg. in adults. In the newborn, Eckenhoff[5] has noted that 0.25 to 0.5 mg. is effective. Excessive stimulation may result from larger doses. It is obvious from the foregoing experiences that the best results were obtained in situations in which a narcotic had been administered to excess and respiratory depression was present, and that the drug is ineffective when respiratory depression is due to other causes.

SUMMARY

N-allylnormorphine, a substance prepared by replacing the methyl group on the nitrogen of morphine by an allyl group, appears to be effective in overcoming depression due to an excess of morphine and other narcotics. The drug is available under the proprietary name of Nalline. It causes no further significant depression when used in doses of 10 mg. or less in adults, when the depression is not due to narcotics. The restorative action remains sustained in cases in which the drug is effective. It is ineffective in overcoming depression due to barbiturates, anoxia, or other causes. It was used in over forty-eight surgical patients who had received an excess of narcotics or who were suspected of having received an excess. In instances in which definite evidence of an excess of morphine or other narcotics was present, the drug appeared to be an effective restorative; in others its behavior was variable. The drug is worthy of further clinical trial and investigation.

REFERENCES

1. Unna, K.: Antagonistic Effect of N-Allyl-Normorphine Upon Morphine, J. Pharmacol. & Exper. Therap. 79: 27-31, 1943.
2. Hart, E. R., and McCawley, E. L.: The Pharmacology of N-Allyl-Normorphine as Compared With Morphine, J. Pharmacol. & Exper. Therap. 82: 339-348, 1944.

3. Huggins, R. A., Glass, W. G., and Bryan, A. R.: Protective Action of N-Allyl-Normorphine Against Respiratory Depression Produced by Some Compounds Related to Morphine, Proc. Soc. Exper. Biol. & Med. **75**: 540-541, 1950.
4. Smith, C. C., Lehman, E. G., and Gillfillan, J. L.: Antagonistic Action of N-Allyl-Normorphine Upon Analgesic and Toxic Effects of Morphine . . . Federation Proc. **10**: 335-336, 1951.
5. Eckenhoff, J. E., Elder, J. D., Jr., and King, B. D.: N-Allyl-Normorphine in Treatment of Morphine or Demerol Narcosis, Am. J. M. Sc. **223**: 191-197, 1952.
6. Fraser, H. F., Wickler, A., Eisenman, A. J., and Isbell, H.: Use of N-Allyl-Normorphine in Treatment of Methadone Poisoning in Man, J. A. M. A. **148**: 1205-1206, 1952.

Case Reports

ADENOMATOID TUMORS OF THE EPIDIDYMIS

A Review of Clinical Findings and Report of Two Cases

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EPIDIDYMAL tumors, though relatively rare neoplasms, have been the subject of some twenty papers in the literature of the past ten years (1941 to 1951). Adenomatoid tumors, constituting approximately 50 to 60 per cent of all epididymal neoplasms, especially merit greater attention.

While the incidence of this tumor at the Mayo Clinic[6] has been seventeen patients in more than 800,000 male genitourinary service admissions, the occurrence at this institution of two such cases within a three-year period would seem to indicate that adenomatoid tumors of the epididymis occur more frequently. Robinson[10] states he had seen six such patients in the European Theater of Operations during the war years.

A review of the literature reveals a wide variety of names for this benign tumor—adenoma, lymphangioma, adenofibroma, adenomatoid tumor, mesothelioma, and even adenocarcinoma. Such a multiplicity of names indicates that the true histologic nature and origin of this lesion is controversial. We, like Golden and Ash,[4] shall refer to it in this paper as an adenomatoid tumor, a name which appears at least "morphologically correct and genetically neutral."

While this tumor appears predominantly in the fourth decade, it has been described in men of ages 15 to 78 years. The usual presenting complaint is that of an intrascrotal mass, the size of which has been noted to remain constant for periods ranging from three to thirty years. Although a history of trauma is frequently elicited, its significance is belied by the absence of hemorrhage or necrosis in the surgical specimen. The mass is usually painless and the patient relatively asymptomatic, although a sensation of scrotal weight has been reported in some instances. Coexisting hydroceles have been occasionally described. History of venereal disease is usually lacking. Bilaterality has not been reported, but a two to one predilection for the left side has been noted. The long periods of survival and lack of metastases testify to the benignity of the lesion.

Careful palpation of the scrotal contents reveals a small, rounded, firm mass (usually less than 2.5 cm. in diameter, although Hinman[5] describes a rare specimen measuring 9 by 5 cm.) which is felt to be attached to the epididymis.

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Occurrence of the mass in association with the globus minor has been four times as frequent as with the globus major. A deliberate and careful palpation will reveal that mass can be separated from the testicle and is attached to the epididymis. Pressure on the mass proper is not usually painful. Transillumination will separate the adenomatoid tumor from the epididymal cyst, the former being opaque, the latter translucent. The correct preoperative diagnosis was made in Case 2 after such an examination.

The purpose of describing two additional cases is to emphasize the fact that the diagnosis can be made preoperatively and that treatment should consist of simple excision of the tumor rather than an unnecessary unilateral orchiectomy or, worse still, a radical retroperitoneal lymph node dissection.

REPORTS

CASE 1.—This was the second admission of a 54-year-old tool and die maker who was admitted complaining of an intrascrotal mass present for thirty-one years. The patient noted the mass after he was kicked in the testis in 1918. Although the lesion was constant in size through the intervening years, slight enlargement in the few months prior to admission was reported. Physical and laboratory examinations revealed no pathology other than a firm, rounded mass about 1 cm. in diameter attached to the lower pole of the epididymis. The lesion was not translucent. Under local anesthesia the tumor was exposed through a scrotal incision. A solid nodule, 1 cm. in diameter, was found intimately attached to the head of the epididymis. It was readily separated from the epididymis by blunt and sharp dissection. The epididymis was then reapproximated and, after taking a testicular biopsy, the wound was closed. The postoperative course was uneventful.

*Pathology.**—

Gross: The specimen consisted of a firm, round nodule measuring 2 cm. in diameter, with a pale pink surface. On section, the cut surface consisted of homogeneous, white, glistening tissue which protruded above the thin capsule when cut.

Microscopic: Examination revealed a reticulated network of spaces lined by flattened cells, some of which contained a few castoff lining cells but no red blood cells. Between the spaces there was moderately dense collagen in which fibroblasts and lymphocytes were seen. Small lymphoid follicles were scattered throughout the tumor. The tumor was surrounded by a vascular collagenous capsule.

Examination of the accompanying testicular biopsy revealed normal tubular architecture with basally placed spermatogonia, spermatocytes, and central spermatozoa.

Diagnoses were (1) adenomatoid tumor of the epididymis, and (2) active spermatogenesis in the testis.

CASE 2.—This was the second admission of this 26-year-old, white man. After an appendectomy in December, 1947, the patient noted a small, hard mass in the right scrotum. The mass was painless and the patient disregarded it until August, 1951. A slow increase in size was noted and the patient felt the mass was twice as large. Genitourinary history was negative. Physical and laboratory examinations were negative except for a hard mass measuring 2 by 2.5 cm., rounded and slightly oval in shape, and intimately attached to the lower pole of the right epididymis but not adherent to the testis. The mass was not tender to pressure and was not translucent. The left scrotal contents were normal. No inguinal adenopathy was noted. The patient was operated under spinal anesthesia through a transscrotal incision. An encapsulated tumor mass was found intimately attached to the lower pole of the epididymis by fibrous bands. These fibrous bands were transected and the mass and lower portion of epididymis resected. A frozen section was performed prior to closure. The patient had an uneventful postoperative course.

*We are indebted to Dr. Raymond Yesner, Chief of Pathology Service, Newington Veterans Administration Hospital, for the description of these specimens.

Pathology.—

Gross: The specimen consisted of a smooth, round encapsulated tumor measuring 3 cm. in diameter which, when cut through the center, revealed a glistening, moist, white structure, firm and rubbery in consistency. There were no whorls present or increased vascularity. Attached to the tumor mass were tightly coiled tubules compatible with epididymis. Frozen section revealed adenomatoid tumor without evidence of malignancy.

Microscopic: Tumor of the epididymis revealed an irregular, moderately fine network of cuboidal and flattened cells, occasionally stratified, frequently resembling thin vessel walls. There were also noted strands of smooth muscle present in connective tissue and aggregates of lymph cells in germinal follicle-like formation. Section included a fragment of adjacent normal epididymis.

Diagnosis was adenomatoid tumor of epididymis.

PATHOGENESIS

The multiplicity of names applied to this benign neoplasm attests to the fact its pathogenesis has not yet been finally elucidated. The theories are likewise multiple and each of the three primitive germ cell layers has been designated as the tissue of origin.

The earlier writers considered an epithelial origin most likely. Ewing and Bloodgood classified the large tumor demonstrated for them by Hinman and Gibson[5] as a probable adenocarcinoma and therefore of ectodermal origin. They were at a considerable disadvantage, however, for this tumor was unique in that it showed invasion of the skin. No other instance of such behavior is found in the literature.

An obvious resemblance to angiomatous tissue (see Fig. 1) with lymphocytes in a follicular-like arrangement caused such writers as Willis,[12] Morehead,[9] and Davenport[1] to consider an endodermal origin. Golden and Ash,[4] however, in their excellent review, feel that this resemblance is only a superficial one.

The most popular concept has been that of a mesothelial origin. Masson, Riopelle, and Simard[8] were the first to suggest this derivation and based their opinions upon the fact that adenomatoid tumors were found not only intrascrotally in the male but also in the female in close proximity to ovaries, tubes, and uterus. They therefore postulated a mesothelial anlage, an opinion with which Evans[2] concurred. Longo and his co-workers[7] in their extensive review advanced the probability of mesonephric rather than mesothelial origin because of the fact that these tumors are found along the mesonephron's course and frequently contain smooth muscle (see Fig. 2) and other tissue elements known to be present in the mesonephric anlage. They compared the epididymal tumor with its benign admixture of normal mesonephric tissues to the hamartomas of other organs and suggested that these tumors be called hamartomas of the epididymis.

The heterogenicity of the tumor caused Sworn and associates[11] to label it a mixed tumor of the epididymis. As Morehead[9] pointed out, the tendency has been to interpret these tumors according to the "quantitative tissue variations." Those containing a predominance of lymphoid tissues thus were called lymphangiomas, those composed mainly of muscle, leiomyomas, and so on. It now appears likely that most of these were adenomatoid tumors with a one-sided preponderance.

Fig. 1.

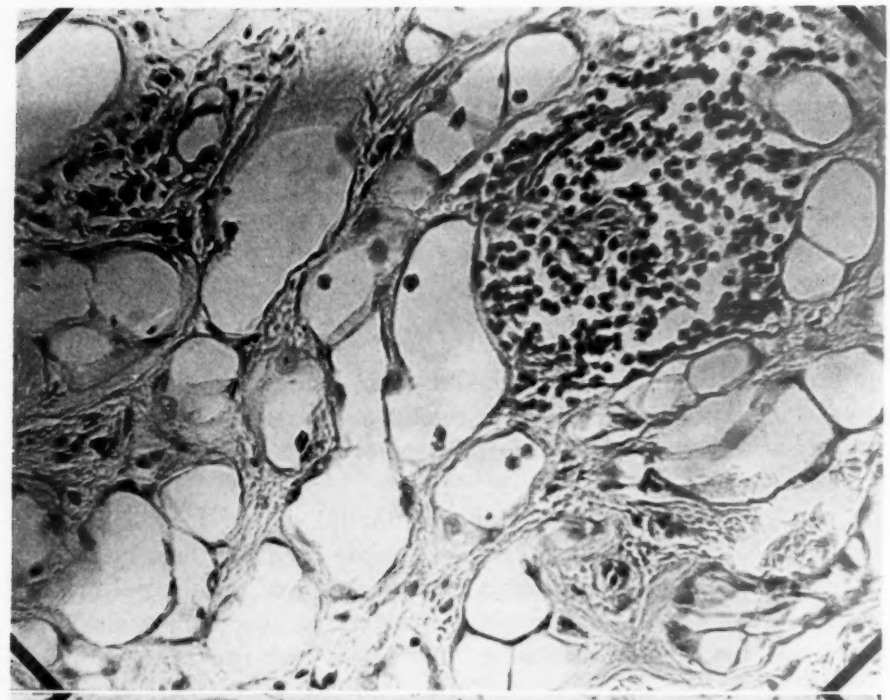

Fig. 2.

Fig. 1 (Specimen, Case 1).—Note lymphocytic follicle-like arrangement and spaces lined by flattened cells.

Fig. 2 (Specimen, Case 2).—Note dense collagenous material and presence of smooth muscle.

An inflammatory basis for the tumor has recently been offered by Falk and Konwaler.[3] Their specimen removed by orchiectomy does not differ markedly in its appearance from the adenomatoid tumor. They base their arguments upon the presence of necrosis and polymorphonuclear leukocytes and the lack of sharp circumscription of the lesion. Lack of sharply defined borders has been noted before in adenomatoid tumors and certainly necrosis and polymorphonuclear cells could be secondary to changes in the tumor rather than of primary inflammatory origin.

SUMMARY

1. The clinical features of the adenomatoid tumors of the epididymis are reviewed.

2. The diagnosis may be made preoperatively.

3. Excision of the tumor only, with conservation of the testicle, is recommended.

4. Two new cases are added to the literature.

5. A brief review of theories of pathogenesis is presented.

REFERENCES

1. Davenport, Harbert: Adenomatoid (Angiomatoid) Formations of the Genital Organs, Texas J. Med. **43**: 694-698, 1948.
2. Evans, Newton: Mesothelioma of the Uterine and Tubal Serosa and the Tunica Vaginalis Testis: Report of Four Cases, Am. J. Path. **19**: 461-471, 1943.
3. Falk, O., and Konwaler, B. W.: Adenomatoid Tumor of Epididymis, J. Urol. **66**: 603-606, 1951.
4. Golden, Alfred, and Ash, J. E.: Adenomatoid Tumors of the Genital Tract, Am. J. Path. **21**: 63-79, 1945.
5. Hinman, Frank, and Gibson, Thomas E.: Tumors of the Epididymis, Spermatic Cord and Testicular Tunics, Arch. Surg. **8**: 100-137, 1924.
6. Lee, M. J., Dockerty, M. B., Thompson, G. J., and Waugh, I. M.: Benign Mesotheliomas (Adenomatoid Tumors) of the Genital Tract, Surg., Gynec. & Obst. **91**: 221-231, 1950.
7. Longo, Vincent J., McDonald, John R., and Thompson, Gershom J.: Primary Neoplasms of the Epididymis, J. A. M. A. **147**: 937-941, 1951.
8. Masson, P., Riopelle, J. L., and Simard, L. C.: Le mésothéliome bénin de la sphère génitale, Rev. canad. de biol. **1**: 720-751, 1942.
9. Morehead, Robert: Angiomatoid Formations in the Genital Organs With or Without Tumor Formation, Arch. Path. **42**: 56-63, 1946.
10. Robinson, I. N.: Benign Tumors of Epididymis and Tunica Vaginalis, Brit. J. Urol. **17**: 68-69, 1945.
11. Sworn, B. R., Marshall, F. W., and Edward, I. L.: Solid Tumors of the Epididymis: Report of Two Cases, Brit. J. Surg. **33**: 375-377, 1946.
12. Willis, R. A.: Pathology of Tumors, London, 1948, Butterworth and Co., Ltd.

TERATOMA OF THE NECK APPARENTLY ARISING IN THE THYROID

Case Report

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A TERATOMA of the neck in a newborn, apparently arising in the thyroid, is of such rare occurrence as to warrant reporting. A total of fifty-seven reasonably authentic cases have been reported. These cases, and the literature, are fully reviewed by Bale.[1]

CASE REPORT

T. S., a 6-day-old female infant, was admitted on Dec. 17, 1951, because of a huge mass in the neck, present at birth. This was the third child of normal parents, and there was no familial history of congenital anomalies. Pregnancy was full term and no hydramnios or other complications were observed. Labor lasted one and one-half hours, and delivery was not difficult, an episiotomy being used. The infant had no respiratory difficulty and was bottle fed, with no cyanosis or choking. On the fifth day the cervical mass was aspirated by needle in three places, there being secured only a small amount of blood.

Examination showed a female infant weighing six pounds, seven ounces (birth weight, seven pounds). The vital signs were normal. The general physical examination was normal except for the neck. Here there was a mass larger than the baby's head, being predominantly anterior although extending well onto each side, particularly on the right where it displaced and distorted the ear. It extended slightly over the mandible above and the clavicles below. It was lobulated and of a soft solid consistence, not definitely fluctuant. The neck was held in hyperextension (Fig. 1).

Routine laboratory data were normal. X-ray examination showed the trachea in its normal position, the mass being anterior to it. There was no calcification. The thorax was not involved (Fig. 2).

On Dec. 19, 1951, under endotracheal ether and oxygen anesthesia, the mass was excised through a long collar incision. The strap muscles were greatly stretched and thinned. There was an excellent cleavage plane around most of the mass. It was attached to the center of the hyoid bone by a stalk of gray tissue grossly resembling thyroid tissue. The blood supply entered posteriorly, but was not definitely identified as thyroid arteries. The mass was removed intact, and inspection then revealed no thyroid tissue at all on the right side of the neck, although there was a normal left thyroid lobe. The parathyroids and the recurrent laryngeal nerve were not seen. The skin was closed without removing any of the moderate excess, and a small drain was left in for twenty-four hours. The baby stood the procedure well, although on three occasions the heart stopped beating momentarily during manipulation in the region of the right carotid artery bifurcation.

Postoperatively the child did well. She was kept in a steam tent for three days to combat tracheal irritation from the endotracheal tube and from manipulation. The cry was a little hoarse, and subsequent laryngoscopy showed paralysis of the right vocal cord, obviously due to operative trauma to the right recurrent laryngeal nerve. Feeding was no problem. After a few days of serous drainage the wound healed solidly (Fig. 3). The

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Fig. 1.

Fig. 2.

Fig. 1.—Before operation. Note the needle puncture marks.
Fig. 2.—Lateral roentgenogram.

Fig. 3.

Fig. 3.—Two weeks postoperatively.

redundant skin will straighten out as the child grows, or, at most, a minor plastic procedure may be needed. The child was discharged on the twentieth postoperative day weighing six pounds, 8 ounces. She was seen several times in the clinic, and on April 23, 1952, the wound was clean with no evidence of recurrence, and the cry was of fair strength with no stridor.

PATHOLOGY

Gross (Fig. 4).—The specimen consists of a lobulated, encapsulated, compressible mass which weighs 270 Gm. and measures 11 by 9 by 8 cm. The color varies from a reddish gray to a brownish black. There are dilated vessels over the surface, which is disrupted at several points. On cut section a 1 to 2 mm. firm, light gray capsule surrounds the entire mass. Most of the tissue is divided into varying-sized lobules, which have an irregular pattern and are distinctly separate. These are composed of a soft, spongy, or friable, yellowish gray substance. Along one edge there are multiple cystic areas ranging from 0.2 to 1.5 cm. in diameter. Some are filled with a clear mucinous fluid while the rest have clotted bloodlike material in the center.

Fig. 4.—Photograph of the external surface and cut section of the gross specimen. Note the lobulations of brainlike tissue with small cyst at upper left.

MICROSCOPIC

With multiple sections through the mass, most of the tissue (at least 90 per cent) is composed of nerve and glial cells situated in a loose fibrillary stroma. Many of the cells are embryonal in type and line irregular cystic spaces (Fig. 5). Several small spaces have a pigmented simple cuboidal epi-

thelial lining suggestive of the choroid layer of the eye. The pattern of this nervous tissue is extremely irregular and bizarre giving an appearance of malformed cerebral cortex. A small portion of the tumor has bundles of smooth and striated muscle as well as adipose and connective tissue but is devoid of cartilage and bone. Small foci of thyroid acini are present but no other organ formation is noted. There are many glandular and cystic spaces which vary in size and shape. These are lined for the most part by simple epithelium, which varies from cuboidal to tall columnar, and is reminiscent of enteric glandular structures. Some of the collapsed spaces have a pseudostratified ciliated columnar epithelium while others a stratified squamous type. Frequently there are abrupt transitions from one type of epithelium to another (Fig. 6). The capsule of the tumor is a dense collagenic fibrous tissue which contains a few lymphocytes and at one point a collection of thyroid acini (Fig. 7).

Fig. 5.—Photomicrograph of the teratoma with both differentiated and embryonal nerve tissue surrounding cystic spaces. Note the pigmented choroid epithelium lining irregular space (center) and the capsule (lower right). Hematoxylin and eosin, ×32.

PATHOLOGIC COMMENT

The diagnosis is teratoma of the embryoid type since elements of all three germ layers are present but without formation of organoid structures. The tumor has no cytologic evidences of malignancy although there are many embryonic cells especially of neuro-ectodermal origin, which always deem an uncertain prognosis. Normal-appearing thyroid tissue is present both within the tumor and the capsule. It is impossible to determine whether the teratoma incorporated thyroid acini while arising from the gland, or it produced the

Fig. 6.

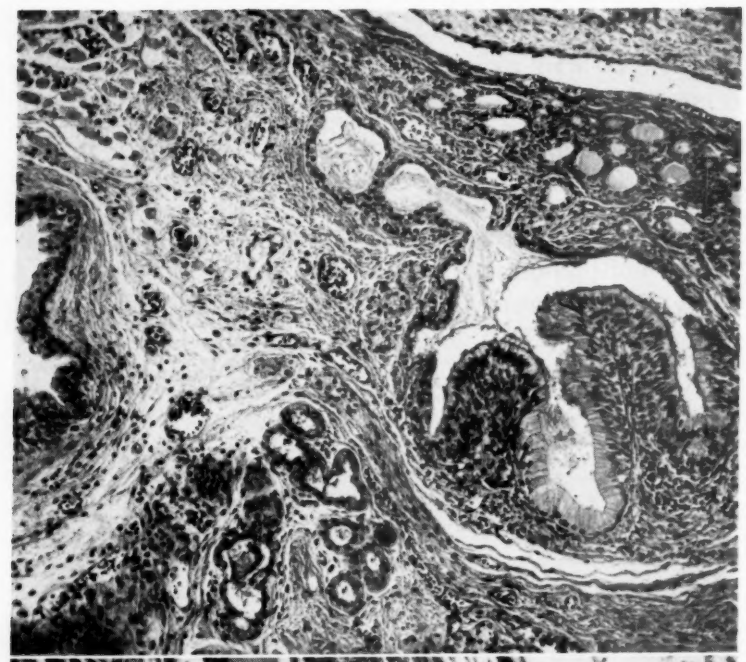

Fig. 7.

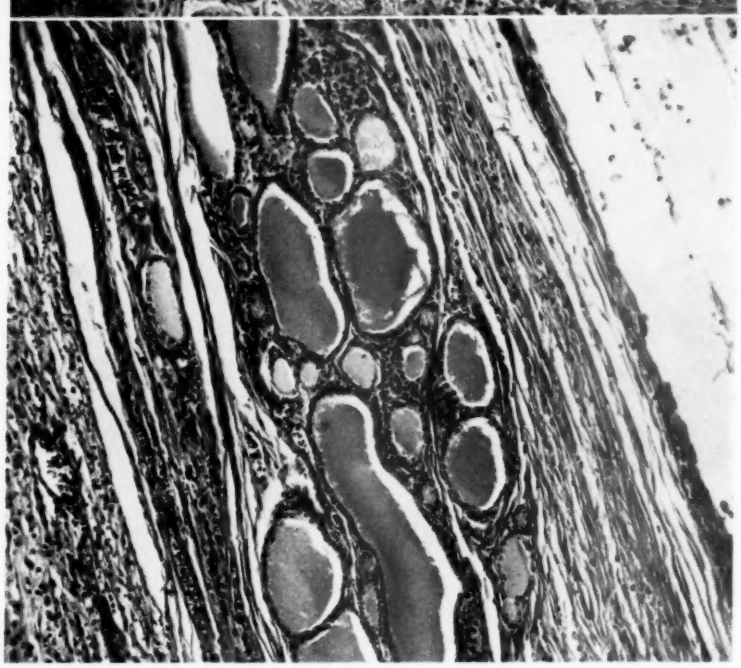

Fig. 6.—Photomicrograph of the teratoma with striated muscle and squamous epithelium (upper left), thyroid acini and nerve tissue (upper right), and glandular structures (lower right and center). Note the transition from cuboidal to respiratory and then to tall columnar epithelium in the largest space (hematoxylin and eosin, ×100).

Fig. 7.—Photomicrograph of the fibrous tissue capsule of the tumor with a collection of thyroid acini (hematoxylin and eosin, ×100).

thyroid tissue per se. Perhaps the absence of the right lobe of the thyroid gland, which was noted at surgery, would suggest the former; but on the other hand the tumor could have produced pressure atrophy.

CLINICAL COMMENT

Two observations mark this teratoma as arising in the right lobe of the thyroid gland: (1) the complete absence of that structure after clean removal of the tumor, and (2) the attachment of the mass to the hyoid bone by a structure grossly typical of the thyroglossal stalk.

In teratomas of the newborn, the cervical location is second in frequency only to the sacral. The sexes are about equally represented. Hydramnios has occurred in eleven of the reported cases. Only in three cases have patients proved to be clinically malignant. The initial clinical impression is frequently that of cystic hygroma, and x-ray is helpful in the differential diagnosis since cystic hygroma tends to surround, infiltrate, and displace the trachea and other cervical structures and frequently extends through the thoracic inlet. Needle aspiration of these masses is of questionable value and should be discouraged.

The treatment is surgical excision as soon as possible. The first operation of this type was performed by Schimmelbusch in 1894, with apparently a cure. The youngest patient operated on was three days old. Of the fifty-eight reported cases, including our case, thirty-one were operated upon, with twenty-seven apparent cures, although the follow-ups were short. Four operated patients died, two of unknown cause, one several hours postoperatively of unknown cause, and the last, a 41-year-old woman, died one month postoperatively of metastases. Of the twenty-seven patients not operated upon, two were dead-born fetuses, ten were stillborn infants, thirteen were newborn infants who lived only a few days, one was a child who died, at age one month, of suffocation due to the mass, and one was a 53-year-old woman who died of metastatic sarcoma presumably arising in the teratoma. From these figures, we see that of the forty-six patients born alive, thirty-one (67 per cent) were operated upon. Considering these thirty-one operated cases, the presumed cure rate was 87 per cent and the mortality rate 13 per cent. If there is no strong contraindication, operation should not be delayed, especially when the mass is large or is interfering with respiration. Newborn infants are good operative risks.

SUMMARY

The fifty-eighth reported case of teratoma of the neck in the newborn, presumably arising in the thyroid, is described. The treatment is surgical removal as soon as possible

ADDENDUM

Since submission of this paper for publication, four additional cases of teratoma of the neck have been reported by D. C. McGoon: Teratomas of the Neck, S. Clin. North America 32: 1389, 1952.

REFERENCES

1. Bale, G. F.: Teratoma of the Neck in the Region of the Thyroid Gland, Am. J. Path. 26: 565, 1950.
2. White, R. R., and Gosselin, R. S.: Teratoma of the Neck in a Newborn Infant, Pediatrics 9: 565, 1952.

THE TREATMENT OF CARCINOMA OF THE ESOPHAGUS BY RADIATION THERAPY AND SURGERY

Case Report

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TREATMENT of true epidermoid carcinoma of the esophagus, as distinguished from carcinoma of the fundus of the stomach with extension to the esophagus, has been relatively unsuccessful. Obvious factors which contribute to the poor prognosis are: (1) the failure of early diagnosis, (2) the fact that the esophagus is a muscular structure with constant waves of contraction which tend to spread the tumor rapidly just as with carcinoma of the tongue, and (3) the lack of a serosal covering to limit spread of the tumor.

Even in the hands of the most experienced surgeons in this field, the cure rate by surgery remains very low. Sweet[1] has reported twelve survivors from 390 referred patients (3 per cent), and of these twelve, eleven were in the lower one-third. Only 0.9 per cent of patients of his operated mid-third cases have survived five years. In those series reporting all patients from a general hospital the five-year survivals have been negligible or completely lacking and even two- or three-year survivals have been few. Parker, Hanna, and Postlethwaite report only one three-year survivor of 170 patients seen.[2] In our own cases no patient with true carcinoma of the esophagus (excluding adenocarcinoma arising from or in the region of the fundus of the stomach) has survived five years.[3] Similar results have been reported by Wu and Laucks from their experience in Peking, China.[4] There are several obvious reasons why the results of surgical treatment would be expected to be poor, except in the lowest portion of the esophagus. An ideal cancer operation with removal of adjacent structures and the lymphatic drainage in continuity is a virtual impossibility because of the intimate vital structures, such as the heart, aorta, or other great vessels, and the hila of the lung. Fleming[5] in a careful study of cases of carcinoma of the esophagus found that of all lesions more than 5.1 cm. in length, 95.5 per cent had gross lymphatic or distant metastases at post mortem.

Radiation therapy either by radium bouginage, interstitial radiation, or external radiation with multiple ports or the rotating chair has also given disappointing results. Using bouginage Guisez[6] treated 270 patients with three five-year survivors (1.1 per cent). Other workers have been unable to repeat these results. Köhler,[7] using crossfire radiation of 5,000 to 6,000 r. in thirty to

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forty days, reported two five-year survivors of 296 patients (0.7 per cent) treated and he frankly stated 30 per cent were made worse. Krebs and associates,[8] using the rotating chair method with 5,000 to 6,000 r. in thirty to fifty days, had seven living patients of 217 treated, only one over five years (less than 1 per cent) at the time of their report in 1949. Gynning,[9] also using the rotational method, reported much better results (5.7 per cent five-year survivals in seventy-seven adequately treated, carefully chosen cases). The difficulties with radiation therapy are obvious. Only the local lesion and immediately adjacent area can be treated so any significant lymphatic extension will escape.

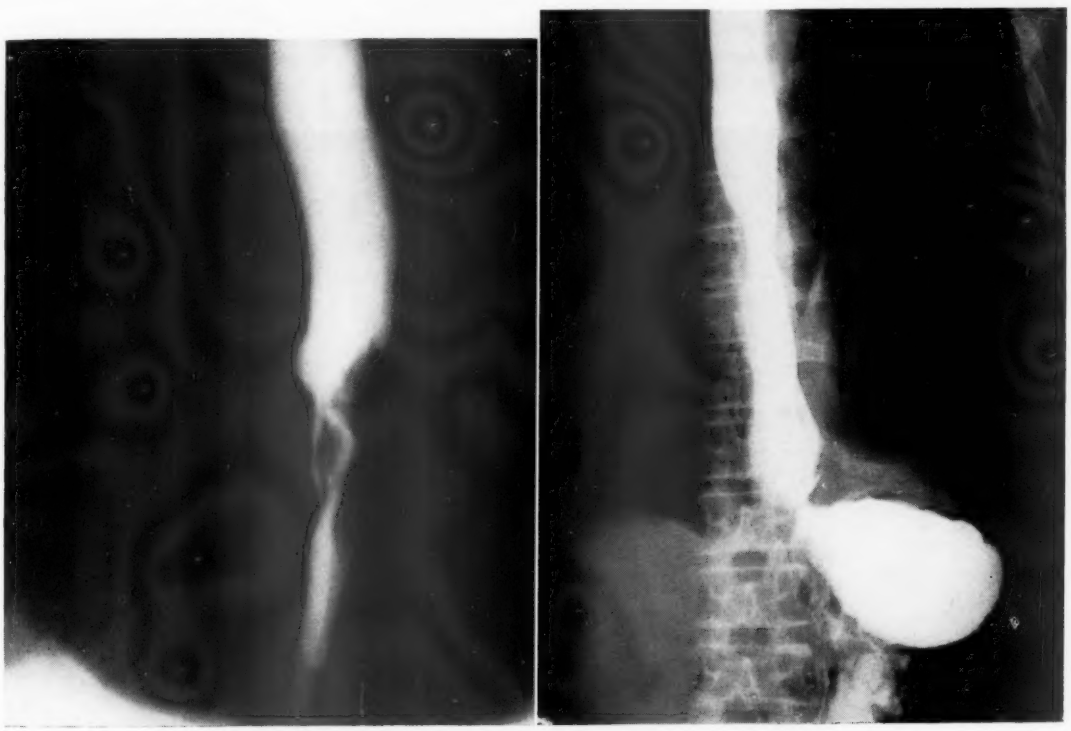

Fig. 1.—X-ray of esophagus in area of lesion (March 16, 1951).

Fig. 2.—X-ray of esophagus in area of lesion, after x-ray therapy has been completed. Note niche on left side of esophagus at level D_8 (July 18, 1951).

Krebs and associates[8] reported an actual disappearance of the local lesion in 20 per cent of cases and yet a very low survival rate. X-ray damage of adjacent structures, particularly the lung, may be disabling and even result in death, and formation of broncho- or tracheo-esophageal fistulas are frequently hastened. Cases of death following x-ray therapy without obvious residual carcinoma at post mortem have been reported by Watson.[10]

Since neither type of treatment is adequate when used alone, as shown by available statistics from outstanding exponents of each, it seems logical to evaluate a combined therapy employing both radiation and surgery. From our review of the literature, it appears that combined treatment of carcinoma of the esophagus by x-ray and surgery has not been reported although such therapy

has been accepted as the treatment of choice for other carcinomas such as the fundus of the uterus[11] and has been used with excellent results in carcinoma of the breast.[12]

CASE REPORT

J. D., a 64-year-old white man, was admitted to New Haven Hospital for the first time on March 10, 1951, with the complaint of progressively increasing dysphagia of three weeks' duration. His admission was precipitated by a large "hemoptysis" and the passage of several tarry stools. Physical examination revealed a fair state of nutrition with no gross stigmata of inoperable carcinoma.

Barium studies of the esophagus undertaken on March 15, 1951, revealed an irregular filling defect 7 to 8 cm. long in the middle one-third of the esophagus (Fig. 1).

Esophagoscopy was carried out on March 21, 1951, and at 33 cm. from the incisors a hard fixed mass was encountered. This was biopsied, and the pathologic diagnosis was anaplastic carcinoma (New Haven Hospital No. SP 53110).

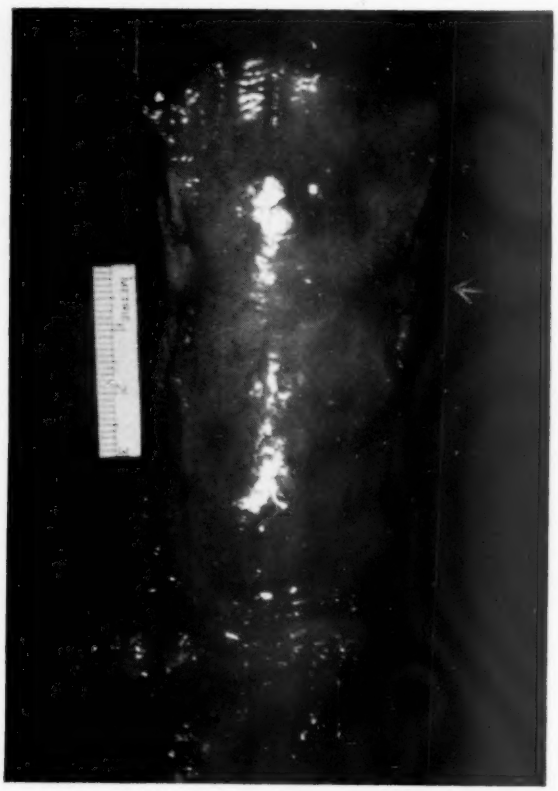

Fig. 3.—Gross specimen, cut longitudinally through the residual lesion. Arrow points to the area of depression in the mucosa.

On April 3, 1951, at thoracotomy, an extensive lesion with its lower margin 10 cm. above the diaphragm was exposed and was found to be fixed to the aorta and to have extended beyond the confines of the esophageal wall into the hilum of both lungs. The lesion was obviously inoperable, after thorough exploration and attempts to free it.

Following an uneventful recovery, x-ray treatment was started, and a total tumor dose of 6363 r., through ten ports, was given from April 12, 1951, to May 25, 1951. There was a rapid therapeutic response, with almost complete disappearance of dysphagia. The patient complained only of incisional pain.

X-ray examination on June 1, 1951, and again on July 18, 1951 (Fig. 2), revealed marked improvement in the appearance of the esophagus with disappearance of the intraluminal tumor and increase in size of the lumen. There was still some narrowing thought to be due to stricture surrounded by a small area of mucosal irregularity suggestive of residual tumor in the middle one-third of the esophagus.

The patient was again subjected to thoracotomy on Aug. 4, 1951, because of the x-ray evidence of marked decrease in the size but still evidence of residual tumor. The esophagus was found to be quite normal grossly except for a 4 cm. segment which appeared thickened and firm 12 cm. proximal to the stomach. Resection of the distal one-third of the esophagus was then carried out, the proximal point of resection being just below the arch of the aorta with a margin of 3 to 5 cm. above the thickened area. Examination of the specimen revealed a small ulceration in the area of thickening (Fig. 3). This area on microscopic section was shown to contain large masses of cells in the submucosa which showed nuclear and cytoplasmic changes compatible with tumor cells affected by x-rays. (New Haven Hospital No. Sp 54351.) Five lymph nodes were examined without evidence of tumor.

Fig. 4.—X-ray showing esophagus, esophagogastrostomy, and thoracic stomach (Sept. 10, 1951).

The patient had an uneventful course and was discharged on his sixteenth postoperative day.

Since discharge the patient has been followed at frequent intervals; he complains of some substernal and epigastric pain on eating, but without dysphagia. Esophagoscopy on Oct. 18, 1951, revealed changes in the esophagus compatible with peptic esophagitis, and no evidence of tumor recurrence. Roentgenograms on Sept. 10, 1951, showed good function of the anastomosis without evidence of tumor (Fig. 4). The patient's symptoms improved on Banthine. Roentgenograms in July, 1952, showed no evidence of recurrence or metastasis. He was last seen in August, 1952, at which time his weight was stable, swallowing was excellent, and his sole complaint was of incisional discomfort.

DISCUSSION

The arguments given against use of the combined treatment include: (1) The x-ray therapy will leave much scar tissue and the operative procedure will be more difficult, if not technically impossible; (2) The carcinoma may metastasize during the period of treatment or in the waiting period after therapy is ended; (3) If the carcinoma is cured by radiation, the operation is unnecessary; (4) Surgical healing will be poor and mediastinitis and empyema may result due to breakdown of the suture line.

The case reported shows that the fear of a difficult operative procedure and poor healing are not necessarily correct. Except for one area of scarring connecting the esophagus to the inferior vein of the left lung no difficulty was encountered and the esophagectomy was very easy by comparison with the usual procedure. So far as healing is concerned, an adequate margin of healthy esophagus was easily obtained; the proximal end (the point nearest to maximum radiation therapy) bled easily and healing was not delayed.

It seems very unlikely that a tumor will metastasize under x-ray treatment. It is more likely that metastases already established would become apparent during or after treatment. The operative morbidity and mortality rates reduced by rejecting patients in whom metastases become obvious during the period of therapy would probably far outweigh the chance of losing a patient.

The argument that the cancer is already cured by radiation and that surgery is therefore unnecessary is not borne out by the available results of the outstanding proponents of roentgen therapy. The false sense of security given by an early favorable response to radiation therapy is shown by the statistics previously mentioned[8]; in 20 per cent of cases there is disappearance of the lesion by x-ray treatment, but only a very few patients survive any significant period of time.

No one can possibly decide in advance which patients have been cured and which patients have a small nidus of tumor cells just outside the radiation field or in an adjacent lymphatic susceptible to removal by an adequate resection. In our reported case it is impossible to say whether the residual cells described were viable. Certainly six weeks after x-ray therapy was concluded cancer cells in significant numbers were still present in the irradiated area.

Even when autopsy reports (Watson[10]) have shown the carcinoma to be completely eradicated, complications such as perforation and abscess formation may still result in death. These might be reduced by early resection after roentgen therapy. In many of those cases presumably inoperable because of the presence of a large mass, or because of extension to adjacent structures, it is probable that subsequent resections would be made easier and the high operative mortality rate decreased.[1, 2]

The possibility of implantation of tumor cells at the site of resection would be minimized by this treatment, both by allowing for more adequate margins or resection and by the well-recognized decrease in transplantability of irradiated cells.

SUMMARY

A case of inoperable carcinoma of the esophagus brought to a resectable stage by preliminary radiation therapy is reported.

The rationale of this treatment is discussed.

REFERENCES

1. Sweet, Richard: The Results of Radical Surgical Extirpation in the Treatment of Carcinoma of the Esophagus and Cardia, Surg., Gynec. & Obst. **94**: 46-52, 1952.
2. Parker, Edward F., Hanna, Charles B., and Postlethwait, Raymond W.: Carcinoma of the Esophagus, Ann. Surg. **135**: 697-708, 1952.
3. Crowley, Lawrence G., and Shedd, Donald P.: Unpublished data from the Tumor Registry, Yale University School of Medicine.
4. Wu, Y. K., and Loucks, H. H.: Carcinoma of the Esophagus or Cardia of the Stomach, Ann. Surg. **134**: 946-956, 1951.
5. Fleming, J. A. C.: Carcinoma of the Thoracic Esophagus; Some Notes on Its Pathology and Spread in Relation to Treatment, Brit. J. Radiol. **16**: 212-216, 1943.
6. Guisez, Jean: Quelques remarques sur le cancer de l'oesophage, Presse méd. **45**: 1135-1137, 1937.
7. Köhler, Rolf: Roentgen Treatment of Cancer of the Esophagus, Acta radiol. **34**: 207-220, 1951.
8. Krebs, C., Nielsen, N., and Andersen, P. E.: Rotation Treatment of Cancer of the Esophagus, Clinical Material, Acta radiol. **32**: 304-316, 1949.
9. Gynning, Inge: Roentgen Rotation Therapy in Cancer of the Esophagus, Acta radiol. **35**: 428-442, 1951.
10. Watson, T. A., and Brown, E. M.: X-ray Therapy in Carcinoma of the Esophagus, J. Thoracic Surg. **22**: 216-218, 1951.
11. Payne, Franklin: The Role of Radiation and of Surgery in the Management of Uterine Carcinoma, Surg., Gynec. & Obst. **94**: 715-721, 1952.
12. McWhirter, R.: Treatment of Cancer of Breast by Simple Mastectomy and Roentgenotherapy, Arch. Surg. **59**: 830-842, 1949.

PARALYSIS FOLLOWING SURGICAL CORRECTION OF COARCTATION OF THE AORTA

Case Report With Autopsy Findings

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INTRODUCTION

PARALYSIS of the legs following the surgical treatment of coarctation of the aorta is apparently a rare calamity. A case in which paralysis occurred seems important enough to report in detail. This case to be described will be the second case in the available literature of paralysis following surgical treatment of coarctation of the aorta. Blalock and co-workers[1] in the report of their first twenty-three cases of coarctation of the aorta treated surgically effected a repair in four instances by anastomosing the end of the left subclavian artery into the side of the aorta. Paralysis of the legs occurred in one case. Blalock felt the paralysis was due to thrombosis of the anterior spinal artery.

Both Blalock and Gross in early studies on the surgical treatment of coarctation emphasized that in the normal dog occlusion of the aorta often caused paralysis of the hind quarters. Blalock and Park[2] in 1943 reported operations on forty-three normal dogs in which they divided the aorta below the left subclavian artery and then implanted the end of the left subclavian artery into the side of the distal aorta segment. Paralysis of the posterior part of the body occurred in almost one-half of these forty-three dogs. The paralysis occurred usually during the first twenty-four hours after the operation. Hufnagel and Gross[6] in their report in 1945 also noted paralysis of the hind quarters in normal dogs in which the aortas had been occluded. There was great variation in the tolerance of the dog to aortic occlusion. In one dog paralysis was seen after ten minutes of occlusion, whereas occasionally there was no paralysis seen in dogs in which the aorta had been occluded for as long as fifty minutes. Crafoord[3] in 1946 reported that he had cross-clamped the thoracic aorta for as long as twenty-seven minutes in patients with patent ductus arteriosus and had not seen any instance of paralysis of the lower one-half of the body.

The pre-ductal type of coarctation in that it occurs close to the left subclavian artery may at times necessitate the occlusion of the left subclavian artery as well as the aorta. A clamp to occlude the aortic arch and still permit left subclavian artery blood flow should be used if possible. Much of the

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collateral circulation above the coarctation occurs through the left subclavian artery. If paralysis were to occur, it could be most expected if the aorta and left subclavian artery were occluded. However, Shumaker[8] in 1951 recommended the use of the left subclavian artery in the repair of certain types of coarctation of the aorta and stated that he knew of no case of paralysis resulting from the occlusion of the aorta and the left subclavian artery.

CASE REPORT

History and Physical Examination.—The patient was a 29-year-old white man who had been in good health all his life until the present illness. He was on active duty in the United States Army for three years from 1942 to 1945. In 1945 at physical examination upon discharge from the Army, the blood pressure in his arm was found to be 200/90. He was otherwise asymptomatic. In 1947 the patient noticed the gradual onset of severe headaches and flushing sensations of face, trunk, and upper extremities. Occasionally, he had vertigo. In 1948 he was admitted to a hospital for study. He was treated with a salt-free diet, sedatives, and nitroglycerin. In February, 1950, while having a physical examination in a Veterans Administration clinic it was noticed that he had absent arterial pulsations in the legs. A diagnosis of coarctation of the aorta was made. He entered the Mt. Alto Veterans Administration Hospital for the first time on March 16, 1950, where he stayed until March 18, 1950. At that time an angiocardiogram was made which showed a 0.5 cm. constriction in the aorta just below the left subclavian artery. He was admitted to the Mt. Alto Hospital for the second time on April 25, 1950, where he remained until May 22, 1950. At that time the decision was made by the Medical Department not to recommend surgical correction of the coarctation. Symptoms were felt to be minimal, and there was only slight evidence of collateral circulation. In the interval after discharge from the hospital the symptoms became much worse. Headaches became more severe. Vertigo became more frequent. The patient developed severe leg weakness which made it impossible for him to work, for he had difficulty in walking for longer than a few minutes.

The patient's family history and past history were otherwise negative. Physical examination at the time of his third admission to the hospital revealed temperature 98° F., pulse 76, respiration 20. The patient was 5 feet, 5 inches tall and weighed 155 pounds. He was a well-developed, well-nourished man in no acute distress. Forceful pulsations could be seen in the region of the carotid arteries. Examination of the heart revealed that it was not enlarged to percussion. There was a grade three systolic murmur heard best at the apex. The blood pressure in the right arm was 158/62 and in the left arm, 160/66. Pulsations in the upper extremities were strong and forceful. No collateral pulsations around the scapulas could be felt. The pulsations in the femoral and popliteal arteries were markedly diminished. No pulsations could be felt in the dorsalis pedis arteries. The blood pressure in the left leg was measured at 90/72 and in the right leg at 112/100. Neurological examination showed normal reflexes and no alteration in sensation.

Laboratory examination revealed that the hematology was within normal limits. Urinalysis was normal. Serology was negative. Blood urea nitrogen, nonprotein nitrogen, total protein, and A/G ratio were all within normal limits. Intravenous pyelograms were normal. Chest roentgenogram revealed the heart to be transverse in position but not enlarged. Minimal waviness was seen about the inferior borders of the ribs five and six, particularly on the right with no distinct notching. The electrocardiogram was normal.

Operation.—The operation was performed on May 10, 1951. The left chest was opened and a constriction in the aorta 0.5 cm. in length was found immediately below the left subclavian artery. The two highest intercostal arteries just below the constricted segment were not dilated. The intercostal arteries below this point were increased in size to approximately 3 to 4 mm. in diameter. The stenosis was dissected free and the ligamentum arteriosum was divided. The two highest intercostal arteries were divided. The left subclavian artery and

the aortic arch proximal to the left subclavian artery were mobilized. Because of the high location of the constriction it was necessary to occlude the left subclavian artery. The clamps were left in place for thirty-eight minutes while the constricted area was excised and an end-to-end anastomosis was carried out using a continuous everting mattress suture of atraumatic 0000 silk. After the clamps were removed, there was found to be a leak in the anastomosis. Five minutes after the aorta had been unclamped, the clamps were reapplied for three to four minutes while an interrupted suture was strategically placed. The clamps were then removed, and two further interrupted silk sutures were placed which completely stopped the bleeding. The chest was drained and the patient returned to the recovery room in relatively good condition. During the operation the patient received a total of 4,000 c.c. of compatible blood twenty-two days old. At no time was the blood pressure in the arms under 100 mm. Hg, and there were no signs of a blood transfusion reaction.

Postoperative Course.—On the first day postoperatively, the patient was alert and felt well. The blood pressure in the arms at that time was 130/80, pulse 120, respiration 30, and temperature 102° F. rectally. He had excellent pulsations in both lower extremities. He had drained approximately 500 c.c. of blood from the chest through an intercostal catheter. The hematocrit was 46 that morning.

It was discovered that the patient had paralysis of both legs. He had intact tactile and position sense in the lower extremities but absent deep tendon reflexes, absent cremasteric reflexes, and absent abdominal reflexes. Intravenous papaverine in doses of 60 mg. was given every four hours. Six hundred thousand units of penicillin was given every twelve hours. The patient was catheterized that day and 750 c.c. of dark brown urine was obtained. The urine was four plus for hemoglobin. The patient, through an inlying catheter, was found to be passing approximately 30 c.c. of urine per hour. He received 3,000 c.c. of fluid this day. No saline solution was given.

The second day postoperatively, the blood pressure in the arm of the patient was found to be 200/100. There were excellent arterial pulsations in both lower extremities. Serum nonprotein nitrogen on this day was found to be 96 mg. per cent with a normal carbon dioxide combining power. There had been a drop in the hematocrit to 36 although the chest drainage had been minimal. The urine contained innumerable red blood cells and two plus albumin. On the third postoperative day, the condition of the patient deteriorated. There were bilateral râles in the chest, and the hematocrit had fallen still further to 26. The oliguria persisted. He received two transfusions of red blood cells suspended in glucose. Later that evening the patient went into acute pulmonary edema which was treated with digitalis and by phlebotomy. The blood pressure in the arms rose to 228/88. The pulse rate was 140. There were at all times good pulsations in the lower extremities. The absent reflexes persisted unchanged. On the fourth postoperative day, there developed unilateral leg edema, and a chest film showed bilateral patchy infiltrations in both lungs. The possibility of phlebothrombosis with pulmonary emboli was considered. The patient received 200 mg. of Depo-Heparin Sodium. On the morning of the fifth postoperative day the patient died from pulmonary edema.

On the first postoperative day the patient received 3,000 c.c. of fluid. On all other days, the total fluid intake was about 2,000 c.c. per day. No saline was administered.

Autopsy.—The left pleural cavity contained 400 c.c. of clotted blood. A blood clot 3 cm. thick surrounded the aorta at the anastomosis. The anastomosis was intact. The heart showed moderate hypertrophy of the left ventricle. The aortic valve was bicuspid with thick, rolled opaque leaflets, but there was no fusion at the commissures. The coronary arteries showed no essential abnormality.

Both lungs showed massive pulmonary edema. The liver and spleen showed moderate passive congestion.

Both kidneys were large, swollen, and pale. Microscopic examination of both kidneys showed many hematin casts in the collecting tubules and loops of Henle, characteristic of hemoglobinuric nephrosis or "transfusion kidney."

The brain and spinal cord showed no gross abnormality. No thrombosis of the anterior spinal artery or other arteries was demonstrated. Multiple sections of the spinal cord were taken at various levels for microscopic study. Pathologic changes in the spinal cord were found from L_3 to S_2. At these levels, the microscopic sections revealed numerous coarse vacuoles in the anterior horns, associated with considerable disruption of the normal architecture (''status spongiosus''). Focal hemorrhages of varying size were present in the anterior horns. Most of the ganglion cells in these areas were in various stages of degeneration and showed pale staining, loss of Nissl substance, and loss of normal processes (see Figs. 1 and 2). The posterior horns and the white matter of the spinal cord did not appear to be involved by the process. Sections of the spinal cord through the thoracic and cervical regions showed no significant microscopic changes.

DISCUSSION

The acute degenerative changes of the anterior horns at the lumbar and sacral levels are interpreted as irreversible damage due to anoxia. The involved area is supplied by the anterior spinal artery. No thrombosis of the anterior spinal artery could be demonstrated, but it is felt that anoxia is an adequate explanation for the lesions. This apparently resulted from clamping off both the left subclavian artery and the thoracic aorta. The subclavian arteries give rise to the two vertebral arteries, each of which gives off a branch to form the anterior spinal artery. Further anastomotic branches from the intercostal arteries and lumbar arteries join the anterior spinal artery. Occlusion of the thoracic aorta would cut off the intercostal and lumbar anastomotic blood supply. Thus, occlusion of the aorta and the left subclavian artery simultaneously would leave only the branch from the right vertebral artery as a source of blood, reducing the blood flow in the anterior spinal artery to one-third or less than normal.

The renal lesion was typical of hemoglobinuric nephrosis. It was probably the most important contributing factor in the fatal outcome, since the resulting disturbance of fluid and electrolyte balance and the anemia probably resulted in the fatal pulmonary edema. Several possible factors may have been concerned:

1. Incompatibility of Transfused Blood.—The patient was type A, Rh positive. All the blood transfused was of the same type. All the bloods were compatible with the patient's blood by the usual cross-matching techniques. However, the transfused bloods were not cross-matched with each other. Cross-matching was not repeated after each separate transfusion. The blood flasks had been discarded when it was realized that a hemolytic reaction had occurred.

2. Volume of Blood Transfused.—It may be important to bear in mind that the volume of blood transfused (5,500 c.c.) amounts to a replacement transfusion in something less than forty-eight hours. Because of this, minor amounts of hemolysis, of no significance in ordinary transfusions, might become of importance.

3. Age of Blood Transfused.—All the blood used was twenty-two days old. The operation was postponed several times to have available a suitable aortic graft. When the operation was finally scheduled, it was impossible to obtain the necessary amount of the Group A, Rh positive blood. The twenty-two day old blood showed no evidence of hemolysis and was considered safe for use.

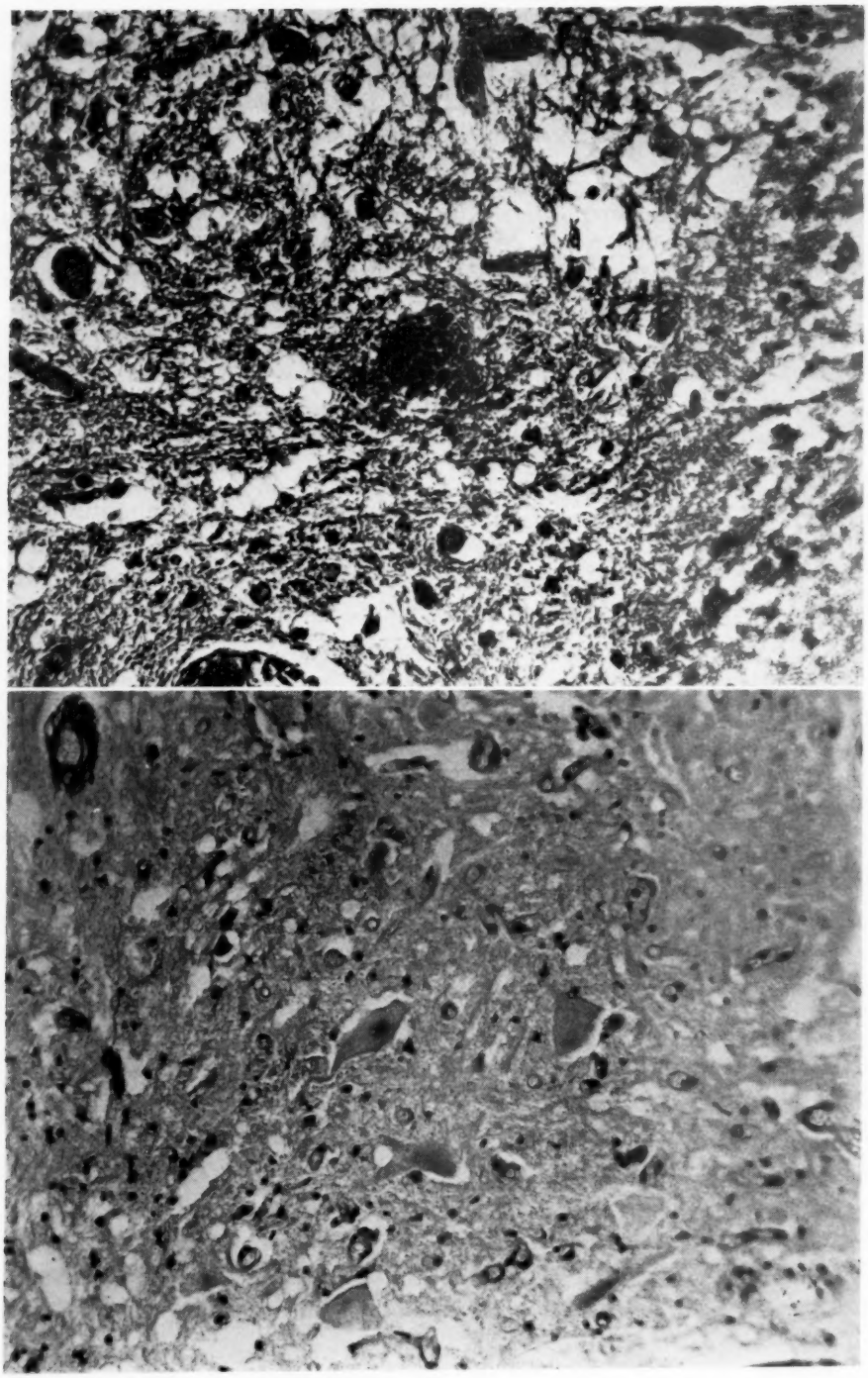

Fig. 1.—Photomicrograph of area from anterior horn of spinal cord at level of L_3. Note distortion of architecture, focus of hemorrhage in center of field and marked vacuolization ("status spongiosus"). Hematoxylin and eosin, ×200.

Fig. 2.—Area from anterior horn of spinal cord at level of S_2. Note degenerative changes of ganglion cells including swelling, chromatolysis, and loss of Nissl substance. Nissl, ×200.

The presence of 10 mg. of free hemoglobin per 100 c.c. of plasma is readily detectable grossly as a red discoloration, which was not present in our bloods. Even if this amount of free hemoglobin were present, it would amount to a total dose of only 550 mg. of free hemoglobin in all the transfusions. It has been shown experimentally by Gilligan and associates[5] that the intravenous administration of hemoglobin to human subjects produced symptoms only when doses of 10 Gm. or more were administered. It would seem clear then that 550 mg. of hemoglobin would be an insignificant amount.

According to DeGowin[4] the hemolysis of 200 c.c. of transfused blood is sufficient to produce serious renal damage. In our case, this would amount to hemolysis of only 3.6 per cent of the 5,500 c.c. of transfused blood. It is conceivable that this amount of hemolysis might occur intravascularly, due to the age of the blood and resulting increased fragility of the erythrocytes.

4. Effect of a Period of Anoxia on the Kidneys.—Clamping of the thoracic aorta produced anoxia of the kidneys. Rosoff and Walter[7] demonstrated that an anoxic kidney would develop hemoglobinuric nephrosis from a concentration of hemoglobinemia insufficient to harm a normal kidney. This apparently happened in our patient.

SUMMARY

A 29-year-old white man was first found to have hypertension in 1945 when aged 23 years. Coarctation of the aorta was not diagnosed until 1950. The lesion was confirmed by angiocardiography. The symptoms were at that time only minimal. The hypertension in the arms was approximately 160/90, and there was only minimal evidence of collateral circulation. It was decided to delay surgical treatment. The patient returned in 1951 with aggravation of the symptoms and extreme leg weakness. It was decided to excise the coarctation. At operation a pre-ductal coarctation of the aorta just below the left subclavian artery was found which necessitated occlusion of the left subclavian artery as well as the aorta. The vessels were clamped for thirty-eight minutes, following which good arterial pulsations were palpable in the lower extremities. On the first postoperative day it was apparent that the patient had paralysis of the legs, although tactile sensation and position sense remained intact. The patient suffered from oliguria and though there was no apparent hemorrhage, his hematocrit fell from 46 on the first postoperative day to 26 on the third postoperative day. The blood pressure in the arms rose. At all times the arterial pulsations in the legs were strong. On the fourth postoperative day pulmonary edema developed, and the patient died on the fifth postoperative day.

At autopsy degenerative changes were found in the lower spinal cord. The kidneys showed hemoglobinuric nephrosis. It seems likely that the calamitous postoperative course was related to the period of anoxia. There was no evidence of incompatible blood transfusion. The blood was approximately twenty-two days old when transfused, and the hemolysis may have been related to the age of the red blood cells. The hemoglobinemia caused hemoglobinuric nephrosis in the anoxic kidney.

This is apparently the second reported case in which paralysis resulted from occluding the aorta and left subclavian artery while excising coarctation of the aorta.

REFERENCES

1. Bing, R. J., Handelsman, J. C., Campbell, J. H., Griswold, E. H., and Blalock, A.: The Surgical Treatment and the Physiopathology of Coarctation of the Aorta, Ann. Surg. **128:** 803, 1948.
2. Blalock, A., and Park, E. A.: Surgical Treatment of Experimental Coarctation of the Aorta, Ann. Surg. **119:** 445, 1944.
3. Crafoord, C., Ejrup, B., and Gladinkoff, H.: Coarctation, Thorax 2: 12, 1947.
4. DeGowin, E. L., Hardin, R. C., and Alsever, J. B.: Blood Transfusion, Philadelphia, 1949, W. B. Saunders Company.
5. Gilligan, D. R., Altschule, M. D., and Katersky, E. M.: Studies of Hemoglobinemia and Hemoglobinuria Produced in Man by Intravenous Injection of Hemoglobin Solutions, J. Clin. Investigation **20:** 177, 1941.
6. Hufnagel, C. A., and Gross, R. E.: Coarctation of the Aorta: Experimental Studies Regarding Its Correction, New England J. Med. **53:** 287, 1945.
7. Rosoff, C. B., and Walter, C. W.: The Controlled Laboratory Production of Hemoglobinuric Nephrosis, Ann. Surg. **135:** 324, 1952.
8. Shumaker, H. B., Jr.: Use of the Subclavian Artery in the Surgical Treatment of Coarctation of the Aorta, Surg., Gynec. & Obst. **93:** 491, 1951.

REPEATED SURGICAL ATTACK ON CARCINOMA OF THE SIGMOID COLON

A Case Report

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THE treatment of cancer at the present time must include every effective implement in the armamentarium of the physician. Wangensteen[1-3] has recently advocated the "second look" as a useful aid in the control of certain gastrointestinal carcinomas. He cited patients who have had as many as six "second looks" at six-month intervals. At these subsequent explorations, many patients have exhibited further evidence of metastatic carcinoma that was amenable to surgical extirpation. Following these secondary excisions, some of the patients have failed to show gross evidence of residual carcinoma at the next "look" six months later. Wangensteen's best results with the technique of "second looks" have been in patients with carcinoma of the colon.

The idea that the patient's only chance for cure lies in the first operation must be abandoned. Variation in biologic behavior of different cancers of the same organ and the early results of "second look" management of gastrointestinal carcinoma indicate the usefulness of repeated surgical attack in many instances. The following case is reported because it illustrates the value that may be derived from secondary operations for cancer.

CASE REPORT

Patient A. McC., a white woman aged 37 years, was first seen in the King County Hospital in August, 1947. She had evidence of a partially obstructing lesion of the sigmoid colon.

Operation 1.—On Aug. 29, 1947, she was operated upon for the first time. An encircling and partially obstructing lesion two inches in diameter was found in the upper sigmoid colon. The lesion had the gross characteristics of carcinoma, but there was no gross evidence of metastases in the regional lymph nodes or the liver. Ten inches of sigmoid with the corresponding mesentery was resected and an axial anastomosis was performed. Microscopically the lesion was found to be a moderately well-differentiated adenocarcinoma with some invasion of the muscularis. Mitoses were infrequent (see Fig. 1). There were no regional lymph node metastases seen on microscopic examination. The patient's postoperative course was uneventful.

She remained well until one and one-half years later when she was readmitted because of a partial obstruction of the sigmoid colon.

Operation 2.—On Feb. 9, 1949, the patient was again operated upon. At this time another "napkin ring" type of lesion was found partially obstructing the colon at the site of the anastomosis. In addition, ten to twelve carcinomatous implants were noted on the pelvic peritoneum overlying the uterus and ovaries. There was also a small nodule of

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carcinoma invading the anterior abdominal wall at the site of the previous incision. The involved segment of sigmoid colon, the pelvic peritoneum with uterus, tubes, and ovaries, and the involved portion of the abdominal wall were resected. End-to-end anastomosis of the colon was achieved. No other evidence of residual gross carcinoma was found at this time. Postoperative recovery was rapid and the patient remained well and free of detectable carcinoma until four months later. At this time a mass 2 cm. in diameter was discovered in the abdominal scar.

Operation 3.—The patient was again submitted to surgery on June 8, 1949. The abdominal-wall mass was found to be adherent to a segment of ileum. Peritoneal exploration revealed no further carcinoma. The abdominal-wall mass was resected in continuity with the involved segment of ileum. Again the recovery was uneventful, and the patient remained well for twenty-seven months. At this time another mass 3 cm. in diameter was discovered deep in the abdominal scar.

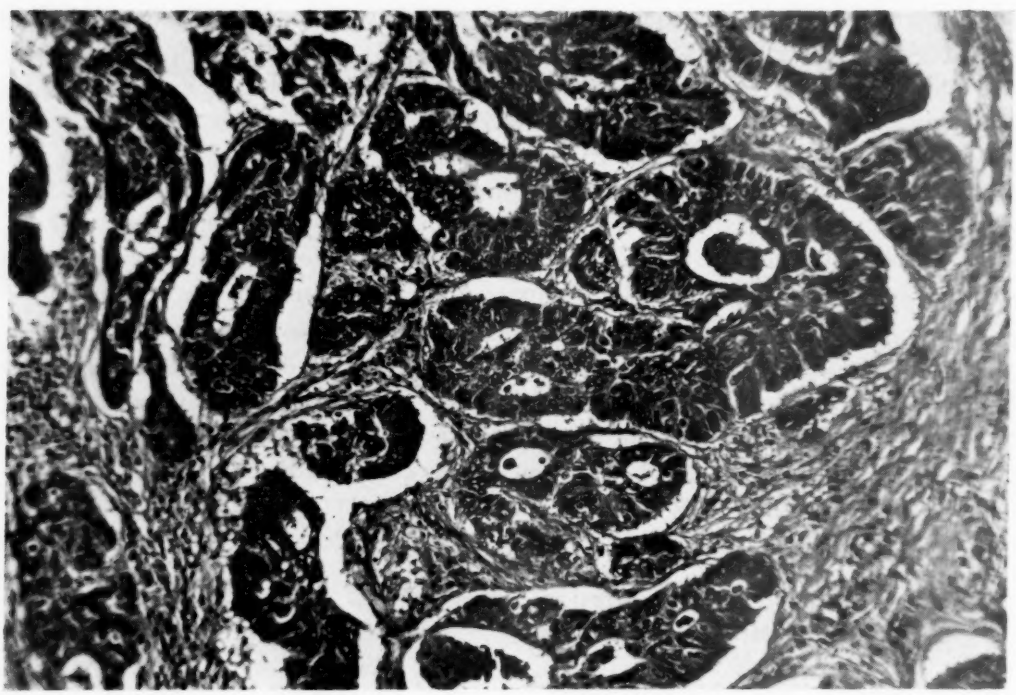

Fig. 1.—Photomicrograph of the original carcinoma removed on Aug. 29, 1947. Hematoxylin and eosin, ×150.

Operation 4.—On Sept. 12, 1951, the abdomen was again explored. The abdominal-wall mass was found to be attached to the dome of the urinary bladder. The involved portion of the bladder was resected in continuity with the abdominal-wall mass. Carcinomatous nodules were discovered in the gastrocolic omentum, in the remaining sigmoid colon, and on the surrounding pelvic peritoneum. The surgeon did not feel that any more should be done at that time. The patient developed a severe wound infection and her hospital stay was prolonged because of this infection. After complete wound healing she was re-evaluated by the tumor clinic. It was felt that she should be re-explored with removal of any persistent tumor that was amenable to resection. Because of the apparent slow-growing characteristic of this tumor and the continued well-being of the patient, further operation seemed justified.

Operation 5.—On Feb. 14, 1952, re-exploration revealed that the upper pole of the spleen was replaced with carcinoma. The liver was grossly normal, but there was a small nodule on the greater curvature of the stomach with involvement of the pancreatic tail and

the left side of the transverse colon. There was another small nodule in the anterior abdominal wall scar and an enlarged lymph node in the ascending mesocolon. All of these areas of involvement were resected in continuity except for the right mesocolic node and the abdominal-wall nodule. These were excised separately. The spleen with metastatic carcinoma is shown in Fig. 2. The surgeon could find no evidence of other residual carcinoma.

The patient's general condition was considered good. She was carrying on normal activity and had no particular complaints. Her normal weight was well maintained at 115 pounds. Two months later, however, another nodule was palpated in her anterior abdominal wall scar, and she was readmitted to the hospital.

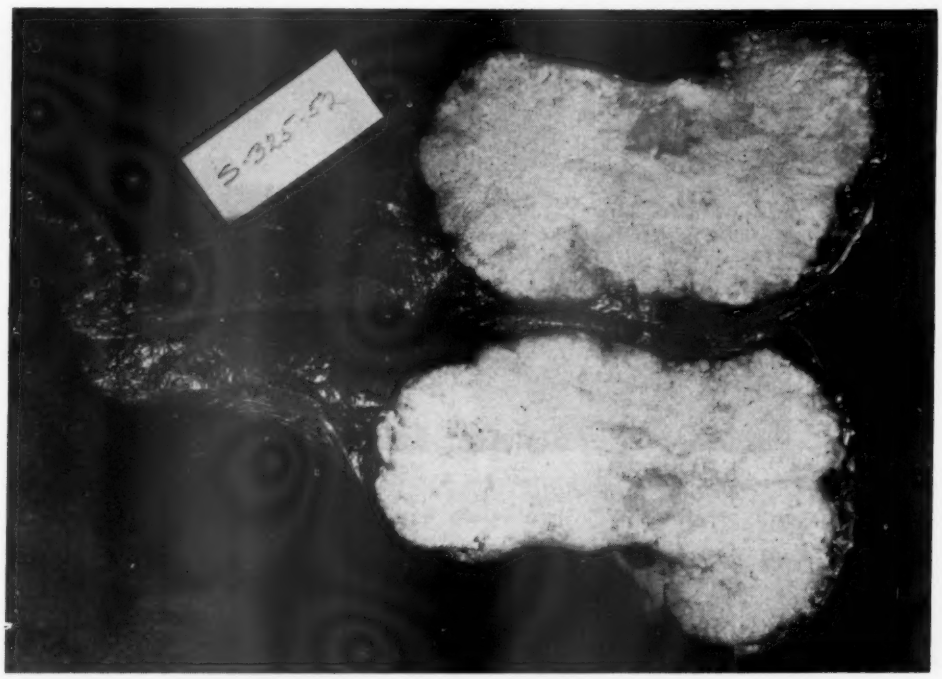

Fig. 2.—Photograph of the spleen containing metastatic carcinoma, removed on Feb. 14, 1952.

Operation 6.—On April 15, 1952, she was again operated upon. No evidence of carcinoma could be found in the upper abdomen. There was a 3 cm. nodule of carcinoma in the abdominal wall, which was adherent to several loops of small intestine. There were about twelve small nodules over the serosal surface of the small intestine involving about five feet of intestine. There was another nodule 2 cm. in diameter involving the descending colon and causing its adherence to the underlying iliopsoas fascia. There was another nodule in the dome of the urinary bladder, and, in addition, there were enlarged nodes along the common and external iliac vessels bilaterally. The following tissues were resected in continuity: 16 square inches of abdominal wall, 6 feet of small intestine, 8 cm. of descending colon, the dome of the urinary bladder, the iliopsoas fascia on the left with overlying peritoneum and bilateral iliac node chains. Intestinal continuity was re-established by axial anastomosis of the small bowel and of the colon. The anterior abdominal wall was repaired with a five-inch square piece of stainless steel mesh (Fig. 3). The postoperative recovery of the patient was rapid. It had been noted on this admission that she had bilateral enlarged inguinal lymph nodes which probably contained metastatic carcinoma. Since this operative procedure had been so extensive, it was felt that inguinal node dissections should be performed only after a period of recovery. Therefore, the patient was discharged for several weeks and re-admitted for the node dissections.

Fig. 3.—Photograph of roentgenogram of the abdomen taken on April 17, 1952. The arrows indicate the stainless steel mesh in the abdominal wall. The barium in the colon was residual from a preoperative barium enema study.

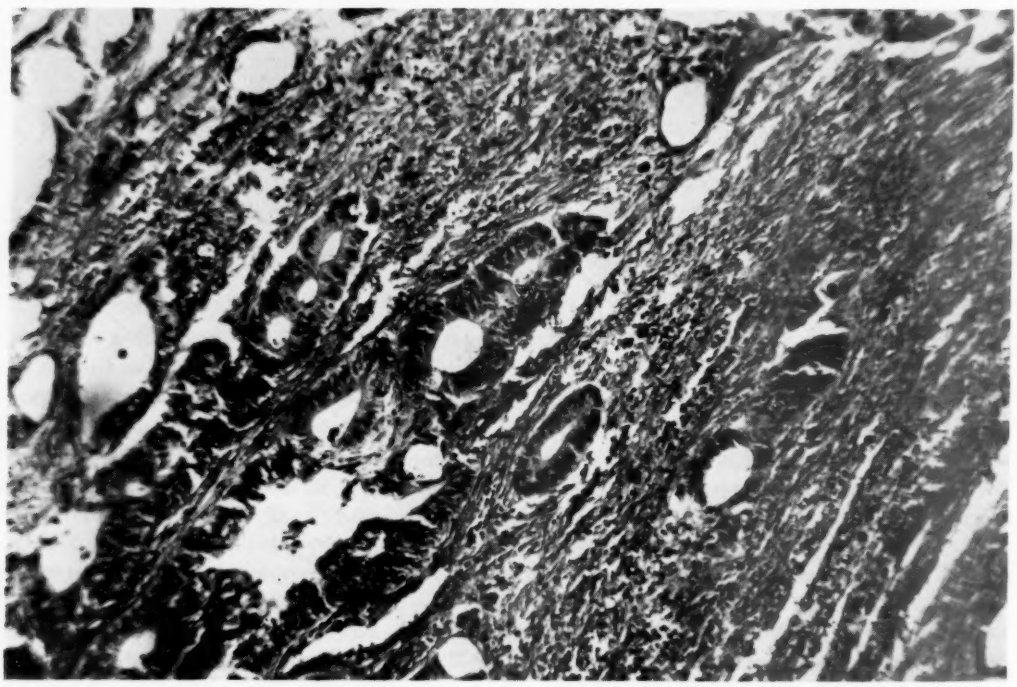

Fig. 4.—Photomicrograph of the metastatic carcinoma in the right inguinal lymph nodes, removed on May 14, 1952. Hematoxylin and eosin, ×150.

Operation 7.—On May 14, 1952, a radical inguinal node dissection was performed on the right. Fig. 4 shows the metastatic carcinoma found in the lymph nodes.

Operation 8.—On May 21, 1952, the left inguinal nodes were resected and were found to contain carcinoma.

The patient has been followed closely in the tumor clinic. She was last seen on Feb. 5, 1953, eight and one-half months after her last operation and five and one-half years after her first operation. At this time she was carrying on her normal activity and had no complaints except for mild leg edema (probably due to the inguinal node dissections). She weighed 113 pounds (preoperative weight, 115 pounds). The abdominal wall showed no evidence of weakness and the stainless steel mesh had caused her no discomfort.

One month before her last clinic visit she had influenza and lost some weight. She developed anemia with a red blood count of 1.8 million. She was given oral iron and vitamins, and at the time of her last visit the red blood count had risen to 3.2 million. Since she has been taking iron, she has had mild diarrhea. There has been no evidence of occult blood loss.

Just prior to this writing, when the patient was last seen in the clinic (Feb. 5, 1953), there was no evidence of persistent carcinoma from history or physical examination.

COMMENT

There is no doubt that this patient would be either dead or moribund from her carcinoma if she had not had the series of operations described. Probably she has not been cured, but she has been given a degree of palliation that has enabled her to live a normal life to the present time. Perhaps the next step in her management should be an elective additional "second look."

SUMMARY

A case has been presented to support the contention that repeated surgical attack on some persistent gastrointestinal carcinomas is a useful method of management.

REFERENCES

1. Wangensteen, Owen H.: Discussion of paper by Lahey, Frank H. and Marshall, Samuel F.: Should Total Gastrectomy Be Employed in Early Carcinoma of the Stomach? Ann. Surg. **132**: 540-565, 1950.
2. Wangensteen, Owen H.: Cancer of the Esophagus and the Stomach, New York, 1951, The American Cancer Society, Inc.
3. Wangensteen, Owen H.: Cancer of the Colon and Rectum With Special Reference to (1) Earlier Recognition of Alimentary Tract Malignancy; (2) Secondary Delayed Re-entry of the Abdomen in Patients Exhibiting Lymph Node Involvement; (3) Subtotal Primary Excision of the Colon; (4) Operation in Obstruction, Wisconsin M. J. **48**: 591-597, 1949.

Editorial

The Place of Pediatric Surgery in Surgical Training

Each year an increasing number of medical students evidence interest in pediatric surgery as a surgical career. This number is out of proportion to the opportunities which exist for such surgical specialists, and it is fitting that some effort be made to see the specialty of child surgery in its proper perspective.

The specialty of child surgery needs no justification, but it should be pointed out that less than fifty men in the Western Hemisphere limit their surgical endeavors to childhood. Many surgeons have a special interest in pediatric surgery, but few make it their major pursuit.

In the six years that the University of Pennsylvania has sponsored in its department of surgery a division of child surgery, we have said as often as possible that the surgery of childhood should not be performed only by pediatric surgeons, but that such pediatric surgeons had something to offer patients and the profession which they did not have before they limited their surgical interest to childhood.

The pediatric surgeon soon develops a close relationship with his pediatric colleagues. He begins to see his patients with a pediatrician's viewpoint and soon is looking toward improvement in the management of problems which formerly would have represented too small a part of his obligation to seem worth while.

A consideration of the place of pediatric surgery raises many questions. How should the pediatric surgeon be trained? What can he contribute to patient care that is not already available? What role does he play in the training of young surgeons?

Just as a surgeon should be a physician and something more, the pediatric surgeon should not be less well trained than the general surgeon. He must be a well-trained surgeon first, and then develop the particular techniques and knowledge in the limitation of his specialty. For the individual who hopes to devote full time to child surgery, two years out of five should be as long as he should spend away from adult training. A much shorter time in special training would adequately equip the man who plans to do most, but not all, of his own pediatric work.

The pediatric surgeon needs all the skill of his general surgical colleagues—and this he can acquire in working with either adult or infant patients—but he also must develop that part of his judgment which is not innate. In my own training, it seemed that the surgical management of patients with concomitant medical disease provided the best opportunity for testing

and improving one's judgment. These situations are less common in children's work than in adult medical practice, and the man who does not spend as much time as possible working with such problems misses much that surgical training has to offer.

There is not unlimited opportunity for pediatric surgeons, but there is a definite place for them in our system of medicine. Every medical school could support a pediatric surgeon, and every children's hospital should have at least one surgeon who lives with the problems of pediatrics closely enough to establish criteria for the care of patients and to provide leadership for his staff in both surgical practice and the field of investigation. In certain instances the medical school and the children's hospital responsibilities can be centered in one office. Pediatric surgeons in these positions are able to introduce medical students to the special problems in the surgery of childhood and can provide resident training.

The surgical management of a patient begins long before his trip to the operating room and continues well beyond it. The surgical service devoted exclusively to the care of children draws not only a variety of cases but also a sufficient volume of unusual problems to encourage the improvement in management on the basis of experience. Such a service is also in a position to attract a house staff which provides not only the backbone of pre- and postoperative care, but in the tradition of American teaching places the senior resident in the role of teacher for his juniors. Finally, the specialty service also draws to itself anesthesiologists who become skilled in the special techniques so important to the successful management of infant surgery. In selected instances, the surgical service for children founded on a broad base enhances the opportunities in the pediatric field for such specialists as the neurosurgeon, the urologist, and the plastic surgeon.

In addition to teaching medical students some of the concepts of child surgery at the grass roots level, the pediatric surgeon is in a position to train young surgeons in the graduate field. For the man who wishes eventually to devote a major portion of his time to children's surgery, the opportunity provided by a children's surgical service is obvious. Residents in training as part of a five-year program in general surgery may, on an affiliating basis, obtain sufficient experience in pediatric surgery to improve the standards of pediatric surgery in their eventual practices. Finally, there is the opportunity to present to visiting surgeons and fellows the experience which may enable them to avoid the pitfalls which lie before the occasional operator in the pediatric field.

—*C. Everett Koop*

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

DUODENAL DIVERTICULA

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INTRODUCTION

ALTHOUGH credit has been given both to Morgagni, in 1765, and to Sommering, in 1794, for the first descriptions, it was Chomel,[10] in 1710, who was the first to describe a diverticulum of the duodenum. Chomel's discovery was rather spectacular in that the lesion contained a calculus, probably as the result of a cholecystoduodenal fistula. The following 200 years produced only a few reports of the lesion, all of them on autopsy findings and, therefore, the clinical features could be reviewed only in retrospect.

Duodenal diverticula were first demonstrated roentgenologically by Case[9] in 1912, and by 1920 six other authors had reported the finding of diverticula of the duodenum by means of the x-ray.

The history of surgery directed at the diverticulum is a relatively recent one, dating back only thirty-six years, for Forssell and Key,[16] in 1915, first surgically removed a diverticulum of the duodenum which had been diagnosed by fluoroscopic examination. This was the first occasion on which a premeditated attack had been made upon the lesion, the diagnosis of which had been made preoperatively, and, therefore, was a very important landmark in the history of the subject.

In recent years more and more attention is being paid to the lesion, probably because of the greater number being discovered by improved means and because of the spreading cognizance of the possibility of the lesion being of clinical importance.

INCIDENCE

As proved by Ackerman,[1] the incidence is much higher than generally is suspected. It is almost impossible to give any figure that would meet with widespread agreement by the various authors, for it appears to vary with the interest of the roentgenologist and the character of the clinic. Also, since the recognition of the lesion has come about comparatively recently, the reported series have been small, and small differences in the numbers, therefore, have given large differences in percentages. In a series of 103 cases reported from the Peter Bent Brigham Hospital and seen over a space of twenty-seven years, it was found that 2.3 per cent of all patients *with x-ray evidence of gastrointestinal disease* had duodenal diverticula. According to Finney,[14] 1 to 1.5

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per cent of all people have duodenal diverticula. The percentages quoted by the different workers, and based on x-ray examination, range from 0.016 per cent by Rankin and Martin[31] to 5.3 per cent as reported by Browne and McHardy.[8]

TABLE I. INCIDENCE OF DUODENAL DIVERTICULA AS REPORTED IN THE LITERATURE

AUTHOR	PER CENT
Rankin and Martin	0.016
Bristow	1.2
Larson	1.6
Beals	2.2
Spriggs and Marxer	5.19
Browne and McHardy	5.3

In the series being reported in this work, patients were observed over the period from July, 1948, through December, 1950. During this time, upper gastrointestinal x-ray studies were carried out on 1,560 patients, ninety of whom were found to have one or more diverticula in the duodenum. The percentage obtained, therefore, is 5.76 per cent. This, it must be borne in mind, is a percentage of the patients with symptoms referable to the gastrointestinal tract who had duodenal diverticula, and is not an accurate measure of the percentage of the population as a whole that may have diverticula. In this regard it is Ackerman[1] who gives the most interesting—and surprising—information. He chose fifty cadavers at random, and made careful studies of the duodenum in each one by the special method of making a mold of the organ in situ. Eleven specimens in his series were found to have diverticula, thus giving the high figure of 22 per cent, the highest on record to the present date. He attributes this to his method of study, stating that many were so hidden in the substance of the pancreas that they surely would have escaped his attention if he had studied his specimens by any other method. This is borne out by a case found at autopsy in this series. On first inspecting the duodenum a small diverticulum was clearly visible. However, on careful examination later, no signs of the diverticulum could be found. It is possible that if Ackerman's method had been followed the diverticulum would not have been lost. It is, therefore, perfectly safe to state that as methods of study improve, the figure quoted by Ackerman will be approached, and it will be possible to make a truer estimate regarding the actual incidence of duodenal diverticula. It is not surprising to note that the incidence reported by authors who base their reports on findings at autopsy examinations is much higher than that reported by those who base their reports upon the results of x-ray studies. In the various reports of such cases the figures vary from 3 per cent to 22 per cent. Since the interest in this clinic was aroused in duodenal diverticula, the incidence has increased. This may be attributed to the exercising of greater care in studying the duodenum during the carrying out of upper gastrointestinal x-ray series.

In this series, 1,560 gastrointestinal x-ray studies were carried out, which resulted in the discovery of ninety patients, or 5.76 per cent, with diverticula

of the duodenum. This is the highest figure reported among the series based upon x-ray examinations.

Table II reveals the considerably higher figures obtained in autopsy reports, and this verifies the assumption that roentgenograms are efficient in diagnosing only a minority of the duodenal diverticula. This fact should be borne in mind, for it may be of importance in the symptomatology of this condition, for a diverticulum which may be causing symptoms may be of a size or in a position that precludes its positive diagnosis by roentgenologic means. In this series, three diverticula which had not been seen on previous x-ray examinations were discovered at operation. These diverticula were incidental findings, and the patients had enough gastrointestinal disease apart from the diverticula (peptic ulcer) adequately to explain their symptoms. However, this is of importance in that these diverticula could not be diagnosed preoperatively, and, therefore, other diverticula which may well be causing symptoms may not be found even after a careful and diligent search by the roentgenologist. Diverticula situated in the third portion of the duodenum usually have their sacs situated superiorly so that they open downward and, therefore, may be difficult to fill with barium.

TABLE II. INCIDENCE OF DUODENAL DIVERTICULA REPORTED AT AUTOPSY AND X-RAY EXAMINATION

AUTHORS	AUTOPSIES	X-RAYS	CASES	PERCENTAGES
Ackerman	50	–	11	22.0
Andrews	–	2,200	26	1.18
Baldwin	105	–	14	13.3
Beals	–	1,887	41	2.2
Bristow	–	1,700	20	1.2
Case	–	6,847	85	1.2
Centano	–	5,263	55	1.04
Cryderman	–	770	40	5.19
Edwards	–	11,362	85	0.75
Grant	133	–	15	11.3
Horton and Mueller	216	–	11	5.09
Larson	–	2,250	36	1.6
Lemmel	–	3,324	50	1.5
Linsmayer	1,367	–	45	3.37
Nagel	–	7,900		2.2
Rankin and Martin	–	72,715	111	0.16
Rosenthal	100	–	3	3.0
Schuppel	45	–	7	15.5
Spriggs and Marxer	–	1,000	38	3.8
Weintraub and Tuggle	–	4,400	104	2.4
Chitambar	–	1,560	90	5.76

AGE

Diverticula of the duodenum have been found in the young and in the old, the patients being drawn from every age group. Grant,[18] of Toronto, working on cadavers, concluded that one person in twenty-five under the age of 52 years has diverticula of the duodenum, while over that age the incidence is as high as one in five or six. From this assumption it may be concluded that the condition becomes established about the fifth decade, and thereafter does

not become progressively more common. The incidence in this series, as the lesion was discovered in patients of the different age groups, is shown in Table III.

TABLE III. INCIDENCE OF DUODENAL DIVERTICULA IN DIFFERENT AGE GROUPS

NO. OF PATIENTS	AGE IN YEARS
0 to 9	0
10 to 19	0
20 to 29	2
30 to 39	1
40 to 49	9
50 to 59	19
60 to 69	29
70 to 79	20
80 to 89	8
90 to 99	0

Although several cases have been reported in the literature, and two patients were found in this series, it is uncommon, but not rare, to find diverticula in patients under the age of thirty. The majority, according to most writers, are seen in the fifth decade of life. However, in this series, by far the greatest number was seen in the sixth decade. The decrease in incidence was fairly even as one advanced to the two higher decades or descended to the two lower decades. Thereafter there was a sudden drop in the incidence. The ages of the patients in this series ranged from 23 to 88 years, the average age being 63.37 years. This average, as compared with that of other workers, is shown in Table IV.

TABLE IV. AVERAGE AGE AT WHICH DUODENAL DIVERTICULA OCCURRED

AUTHOR	AGE IN YEARS
Beals	53.3
Case	56
Edwards	53.8
Finney	63.7
Gibbon	52
Horton and Mueller	60.8
Lawson	51.4
Rankin	55.6
Spriggs and Marxer	55
Warren and Emery	58.07

SEX

The incidence of duodenal diverticula among the two sexes is another point on which there is a difference of opinion. Most authors report a higher incidence among men, but reports stating that the incidence is higher in women are not lacking, while there are several who have drawn the conclusion that duodenal diverticula occur equally among the two sexes. In this study a definitely higher percentage of the patients were women. Of the ninety patients, fifty-one or 56.67 per cent were women, and thirty-nine or 43.33 per cent were men. This preponderance of women is borne out also in

cases seen in this clinic in the five-year period prior to the dates covered by this series. The percentages reported by the various authors are given in Table V.

TABLE V. OCCURRENCE OF DUODENAL DIVERTICULA ACCORDING TO SEX

AUTHOR	MEN (PER CENT)	WOMEN (PER CENT)
Case	40	60
Centano	67	33
Edwards	37.5	62.5
Horton and Mueller	63.9	36.1
Hahn	46	54
Herbst	58	42
Rankin	73	27
Spriggs and Marxer	47.3	52.7
Warren and Emery	37.86	62.14
Weintraub and Tuggle	45.48	54.52

LOCATION

The duodenum has been divided into three portions by some writers and into four portions by others. In this study the duodenum has been regarded as consisting of three portions. The descending portion of the duodenum constitutes the second part. Between the pylorus and the second part, and distal to the descending portion, lies the first portion; that is, the transverse and ascending portions constitute the third part of the duodenum.

In this series, the majority of the diverticula were found to be located in the second portion of the duodenum. On this point there is general agreement throughout the literature. Of the one hundred diverticula in this study, sixty-six or 66 per cent were found to arise from the second portion of the duodenum. All but two of these arose from the concave or inner border. The remaining two arose from the lateral or convex border, and were situated in the vicinity of the junction between the second and third portions of the duodenum. Twenty-two, or 22 per cent, of the diverticula were present in the third portion of the duodenum, while the smallest incidence, 12 or 12 per cent, was found in the first portion. These findings are in general agreement with those of other authors, although they all report a smaller incidence in the first portion, and some of them go so far as to say that diverticula are not found in the first portion of the duodenum.

TABLE VI. LOCATION OF DUODENAL DIVERTICULA

AUTHOR	FIRST PART	SECOND PART	THIRD PART
Ackerman	0	6	8
Baldwin	0	15	0
Beals	0	28	17
Browne and McHardy	3	29	13
Case	17	49	19
Centano	0	37	17
Edwards	0	22	9
Gibbon	1	12	8
Lawson	8	16	12
Weintraub and Tuggle	6	248	90
Total	35	462	193
Per cent	5.07	66.95	27.98

It is generally agreed that by far the greatest number of diverticula occur in the second portion of the duodenum, and, of these, almost all arise from the inner aspect or concave border of the descending portion in close proximity to the head of the pancreas. However, the statement made by Mahorner,[25] that diverticula are invariably found on the side of the blood supply, is untenable, for the diverticula discovered in this series arose from both superior and inferior aspects of the first part, medial and lateral aspects of the second part, and superior and inferior aspects of the third part of the duodenum (Figs. 1 to 5).

ETIOLOGY AND PATHOLOGY

The origin of diverticula of the duodenum is still a controversial issue. The diverticulum is an outpouching of the duodenum, a herniation of the mucous membrane through a spot of lowered resistance in the duodenal wall. The condition, according to Boyd,[6] is in the nature of an aneurysm. The mucosa and muscularis mucosae are protruded through the muscular layer, so that the wall of the sac most often is composed only of these two layers. Boyd believes, therefore, that the causes of the formation of duodenal diverticula, although obscure and probably complex, are akin, at least in part, to the production of aneurysms. The two most important factors would appear to be a weakening of the wall, and an increase in the pressure within the bowel. To these may be added traction from without. The various factors which are believed to play a part in the production of duodenal diverticula are:

A. The area of weakness in the duodenal wall being at the point of entry of the small vessels through the muscular coat where fat may be seen entering the wall and reaching the submucosa. This is the most generally accepted theory and is borne out by the fact that almost all primary diverticula are found on the concave aspect of the duodenum, on the mesenteric side where the vessels enter. However, although this factor is recognized as the most important etiologic factor, the assertion of Mahorner that diverticula are invariably found on the side of the blood supply cannot be accepted, for several cases have been reported, and some were seen in this series, in which the diverticula arose from the opposite side of the bowel. There must, therefore, be other factors that can play a part and, at times, be of importance in the production of duodenal diverticula. Fletcher and Castleden[15] state that the close relationship of the necks of the diverticula to the blood vessels which pierce the concave aspect of the bowel, or to the entry of the common duct, suggests a gradually developing protrusion through the weak spot so formed. Thus, although occasionally found in the young, they are more frequent as age advances. Hansemann[19] feels that it is the course of the veins that decides the location of duodenal diverticula. It would follow, therefore, that venous congestion, increase of pressure, loss of fat, and age would favor their development. The mucosa and submucosa bulge outward into the sheaths of the veins. Occasionally the entire wall is pulled outward by traction of mesenteric scars or tumors in or about the bowel.

B. Weakness caused by the presence of pancreatic rests in the duodenal wall. This theory, put forth by Linsmayer,[23] has been verified in several reported cases in which pancreatic tissue was found in the fundus of the sac.

C. The presence of fat in the muscular layer causing a defect in the musculature and, thus, a weak point.

D. Outpouching of the duodenal wall similar to the anlage from which developed the liver and the pancreas. This is an oft-expressed theory and the possibility of its being an important factor in the etiology of duodenal diverticula is receiving more widespread recognition.

E. Traction either of the pancreatic or common duct, or from the head of the pancreas itself when it has undergone focal or widespread atrophic changes due to chronic interstitial pancreatic disturbances, or from the gall bladder itself in gall bladder disease.

F. Weakness caused by ulceration. This is most common in the first part of the duodenum. All patients in this series who had diverticula in the first part of the duodenum gave a history of perforation of a duodenal ulcer several years previously. In the two patients in this series in whom the diverticula were resected, the resection was carried out in the process of a subtotal gastrectomy for duodenal ulcer. Contrary to what one would expect, in both the diverticulum was a true diverticulum, the walls consisting of all coats of the intestine. Diverticula in this region, though less common than in the second and third portions, when not secondary to ulceration, probably are all true diverticula, and congenital in origin. They possibly represent the anlage of "pyloric coeca," pouches which occur in certain species of fish and which empty into the duodenum (Kyle[21]). According to Hart the scars of ulcers may cause pleating of the mucosa and thus a diverticulum, the outpouching occurring chiefly in the vicinity of the pylorus. Boyd[7] describes secondary diverticula as occurring secondary to duodenal ulceration so that they occur in the first part of the duodenum. There may be a bulging of one or both sides of a healed scar due to traction.

G. Increase of pressure within the duodenum. This is attributed by Keith[20] to enteroptosis and partial obstruction at the duodenojejunal junction. Barnes[3] reports a patient who was operated upon in whom a duodenal trap was formed by pressure by an aberrant vessel. This increase of pressure may be caused by pressure from without by an extrinsic mass. One patient in this series had two diverticula, one situated in the second portion of the duodenum measuring 4 cm. in diameter, and the other, a large diverticulum which was mushroom shaped, in the third portion of the duodenum. Fluoroscopic examination was most spectacular, for the barium would progress as far as the distal diverticulum. The diverticulum and the duodenum then would distend, following which retroperistalsis would be set up and the barium would return into the stomach, some remaining in the diverticula. The process would be repeated over and over again, only small amounts of barium entering the jejunum each time. This patient refused operation for several months, and when she finally did come to surgery it was found that the pressure was being caused by a carcinoma of the pancreas.

Fig. 1.

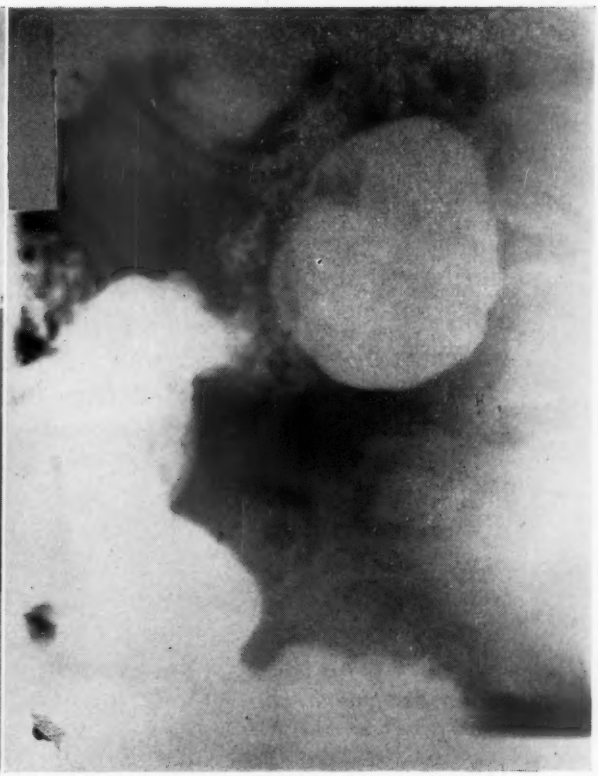

Fig. 2.

Fig. 1.—Large diverticulum arising from the second portion of the duodenum.

Fig. 2 (Same case as Fig. 1).—Large diverticulum of the second portion of the duodenum. Partial twenty-four hour retention of barium and fluid level are well demonstrated.

Fig. 3.

Fig. 4.

Fig. 3.—Diverticulum of the third portion of the duodenum.

Fig. 4.—Two diverticula arising from the second portion of the duodenum.

According to the old classification, diverticula were divided into two groups, the congenital and the acquired. The distinction is most difficult to define, for probably all diverticula, other than those formed by penetration of an ulcer, start out as congenital weaknesses, the diverticula being developed as age advances. Diverticula also have been divided into true and false types. The wall of a true diverticulum contains all layers of the intestine wall, whereas that of the false type does not contain the muscular layer. A false diverticulum is, therefore, a herniation of the mucosa through an opening or weakness in the muscular wall. A pseudodiverticulum caused by penetration of an ulcer is differentiated from other diverticula by the fact that in the latter there is no distortion of the adjacent duodenum.

The old classification of congenital and acquired diverticula now has been largely abandoned, and has been replaced by Odgers'[28] classification of diverticula in two groups—Primary and Secondary. In the latter type the cause is known, but in the former the etiology is obscure.

Beals,[4] Edwards,[12] and Friedlander[17] postulate that all diverticula in the first portion of the duodenum are associated with the presence of peptic ulceration. This has been borne out in this study.

Edwards describes as a distinct entity or group what he chooses to call the ulcer diverticulum. This occurs in the first part of the duodenum and is associated with, but lies at some distance from, the duodenal ulcer. He describes each diverticulum of this variety as containing all four layers in its wall. He states that the lining of the pouch is smooth and that there is no inflammatory process in its wall. These apparently are formed by the shortening of the duodenum by contraction of the scar tissue of the healed ulcer, so that the portion of the duodenum unoccupied by ulcer is puckered up and ballooned outward by intraduodenal pressure to form the diverticulum. Thorek[34] and Turner[35] describe the diverticula caused by the yielding of an ulcer, and they describe cases in which the floor of the diverticulum has been formed by the crater of an ulcer. According to Edwards these views are at variance with one another. However, both these views describe diverticula that do exist, both types of which have been seen and are included in this series.

All the patients in whom diverticula were found by x-ray examination to be situated in the first portion of the duodenum gave a history of a perforated duodenal ulcer several years previously. This penetrating ulcer, when healed, apparently leaves a weak spot in the wall of the duodenum in which the muscle layer is destroyed. This fulfills one of the criteria put forward by Boyd. The second criterion—increased intraduodenal pressure—then plays its part, and the diverticulum is formed. Two patients in this series had diverticula in the first part of the duodenum, in the spot where five and seven years previously gastrointestinal x-ray studies had revealed the presence of an ulcer crater.

Of the diverticula removed from the first portion of the duodenum, one was a good example of the "ulcer diverticulum" of Edwards. All four layers of the wall were intact, the lining of the pouch was smooth, and no inflamma-

tory process could be detected in the wall. Another good example was a female patient who gave a long ulcer history. On x-ray studies of her gastrointestinal tract a definite ulcer crater could be seen, and, in addition, a diverticulum arising from the upper and another from the lower border of the first part of the duodenum. These, apparently, were as a result of the ballooning described by Edwards. The various changes that may take place in a diverticulum of the duodenum are of importance. Several cases of ulceration have been reported, and one such case was seen in this institution and is included in this series.

Fig. 5.—Duodenal diverticulosis.

The second diverticulum to be resected was a true congenital or primary diverticulum of the first part of the duodenum, the type which Edwards calls "excessively rare." All layers in the wall were intact, but a remarkable amount of acute inflammation was present. This patient also had a prepyloric peptic ulcer, and it is conceivable that the same forces were at work in the diverticulum, and that, allowed to progress, they would have gone on to ulceration within the diverticulum. Apparently the outstanding factor in the production of peptic ulcer is the proteolytic action of the gastric secretion upon mucous membrane whose vitality already has been lowered by trauma or interference with blood supply. It is conceivable, also, that small islets of gastric mucosa may be present, and that these may act in a manner identical with the mucosa in normal anatomic position, elaborating the gastric secretion in normal or excessive amounts. This view has been advanced by Weig. Ac-

cording to Ehrenpreis,[13] gastric heteroplasia is said to occur in 12 per cent of Meckel's diverticula, and in such cases peptic ulcers have been found. However, this superficial heterotopia of gastric glands is quite rare, and, therefore, may not be the explanation of the occurrence of peptic ulceration within duodenal diverticula. Interference with blood supply is a known predisposing factor, and it appears logical that at the fundus, especially in a diverticulum of considerable size, there may be an area of vascular insufficiency. In such a case, retention of food particles probably would act as an effective irritant.

There has been no mention in the literature of any familial characteristics of duodenal diverticula. However, in this series there were two sisters in both of whom x-ray studies of the gastrointestinal tract revealed multiple and spectacular diverticula of the duodenum. No definite conclusions can be drawn from this, but the possibility of similar congenital weaknesses occurring in different members of the same family must be recognized. The fact that a congenital local weakness and increase of pressure within the bowel are important predisposing causes is borne out by the finding that duodenal diverticula frequently are multiple. In this series, twelve patients, or 13.3 per cent, had two or more diverticula in the duodenum.

TABLE VII. SINGLE AND MULTIPLE OCCURRENCE OF DUODENAL DIVERTICULA

AUTHOR	SINGLE (PER CENT)	MULTIPLE (PER CENT)
Baldwin	86	14
Browne and McHardy	95	5
Nagel	70	30
Spriggs and Marxer	84	16
Warren and Emery	93.2	6.8

Duodenal diverticula frequently are associated with diverticula elsewhere in the gastrointestinal tract. Twenty-eight patients or 31.1 per cent in this series were found to have diverticula elsewhere in the gastrointestinal tract, while twelve or 13.3 per cent had diverticula in portions of the small intestine other than the duodenum. A point of interest is the incidence of colonic diverticula in patients with diverticula of the duodenum. In this series, diverticulosis coli was discovered in twenty-one patients, thus giving the high figure of 23.3 per cent. This is much higher than the 10 per cent and less, quoted by most authors, but coincides with the figure of 23 per cent put forward by Weintraub and Tuggle.[39] However, its is important to note that of the ninety patients, barium enema studies were carried out only in forty-two. The actual incidence of colonic diverticula in patients with diverticula of the duodenum, therefore, actually approaches the amazingly high figure of 50 per cent.

A frequent association between diaphragmatic (esophageal hiatus) hernia and duodenal diverticula has been noticed in this study. Nine patients or 10 per cent were found to have both duodenal diverticula and diaphragmatic hernia. Duodenal diverticula vary from a few millimeters to several centimeters in size. The largest seen in this series measured 5.7 cm. in diameter. The greater number are globular. Funnel-shaped and cylindric diverticula

are not uncommon, while bilobed and other bizarre-shaped diverticula sometimes are encountered. Bilobed, lobulated, and mushroom-shaped diverticula were seen during the process of this study, while one diverticulum which retained food particles gave the appearance of having scalloped edges. The most spectacular diverticulum, however, was one which was situated in the second portion of the duodenum. This measured 3 cm. in diameter, while from its fundus arose a smaller diverticulum. This double diverticulum retained barium for six hours.

In the majority, the circular and longitudinal muscle coats of the duodenum are missing, and the mucosa and muscularis mucosae make up the wall of the diverticulum. Most of the sacs do not show the presence of any pathologic process other than the saclike process with or without defective muscular layers. However, if the neck is narrow and the diverticulum empties with difficulty, varying degrees of inflammatory reactions may be noted. On x-ray examination it is often impossible to ascertain the exact point of entry of the diverticulum into the duodenum, and in such cases it is difficult to distinguish between a primary diverticulum and an ulcer diverticulum. Edwards points out, as an aid to the differential diagnosis, that if peristalsis is seen in the wall of the diverticulum, it is certain to be of the ulcer type or secondary to ulcer. On the other hand, Pendergrass,[30] in differentiating between redundancies and diverticula, emphasizes the presence of peristaltic waves and serrated outlines in redundancies and their absence in diverticula.

The microscopic picture of the diverticulum is of interest. In the majority at the fundus there is practically no muscle layer except a very thin one, only one or two fibers deep, which represents the muscularis mucosae. This layer may be so well defined as to be thicker than that in the duodenal wall, as in the case of large bowel diverticula. This is due to compensatory hypertrophy because of the deficiency of the muscular layer proper. As examination of the wall proceeds toward the mouth of the sac, the muscle fibers may become more abundant. At the commencement of the neck of the sac the muscular coat of the duodenum is unusually thick. There is then an immediate diminution in thickness of both circular and longitudinal muscle layers, which become more and more attenuated toward the fundus of the sac. They finally disappear entirely or are represented by a layer one or two fibers thick. It is often difficult to decide as to whether this is the muscularis proper or the muscularis mucosae. The mucosa is thinned, but, in most cases in which there is no additional pathologic change, shows no abnormality except the absence of any Brunner's glands. This picture apparently explains the statement made by Baldwin[2] that all fifteen diverticula examined by him were of the "true" type, for they all contained muscle which consisted of a single layer. The diverticula excised from the first portion of the duodenum in this series were both of the "true" type. All layers were intact in the walls, and both specimens showed a well-developed muscular layer even at the fundus (Figs. 6 to 8).

That diverticula will increase in size through the years is a known and undisputed fact. In one case in this series the diverticulum situated in the

Fig. 6.

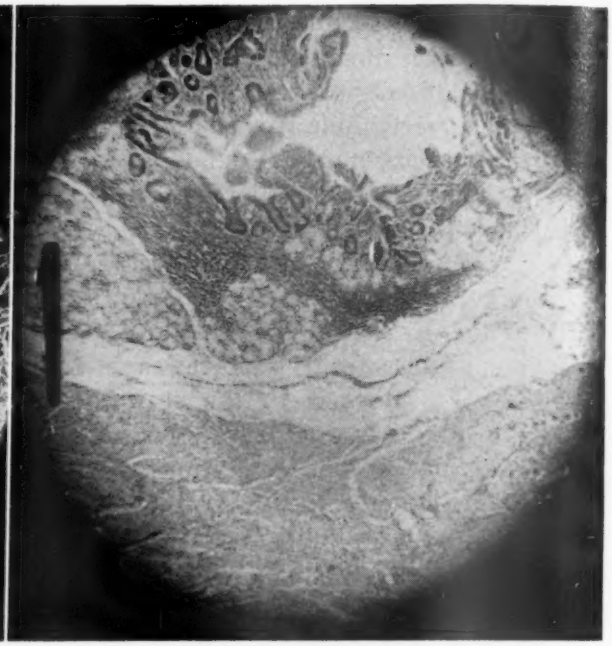

Fig. 7.

Fig. 6.—Section through wall of diverticulum of first part of duodenum to show well-developed muscle layer. Photograph does not include mucosa.

Fig. 7.—Section through wall of diverticulum of first part of duodenum, showing mucosal and well-developed muscle layers.

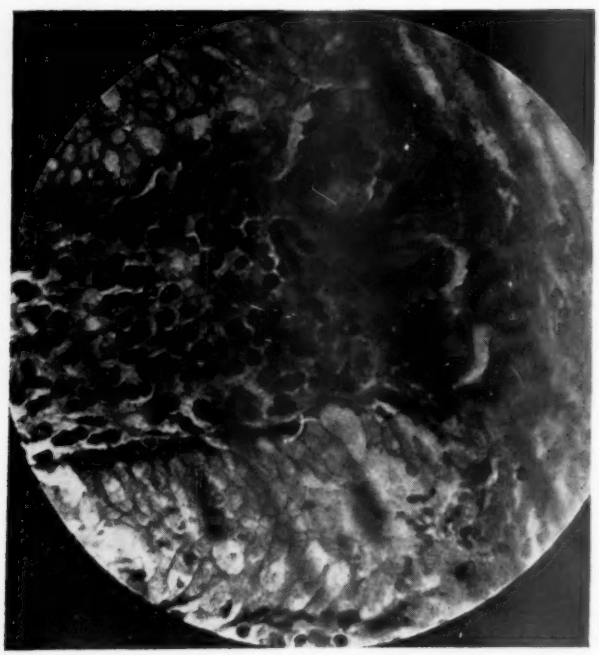

Fig. 8.—Section through projection of mucosa of diverticulum showing inflammation with round cell infiltration.

second part of the duodenum was found to have increased by 2 cm. in diameter over a ten-year period. It is known, also, that diverticula will decrease in size when treated or when for some other reason the various predisposing causes are removed. This being so, it may be logical to assume that when the cause is removed a diverticulum may diminish in size to the point where it disappears altogether. One case was seen in this study in which a small diverticulum of the second part of the duodenum was discovered. This patient was kept under strict ulcer treatment, and two years later, in spite of careful examination, no diverticulum could be identified. It would be dangerous to draw any conclusions from this case, for diverticula are notoriously difficult to find, and, in repeated examinations during the same hospitalization, may be seen at one examination and not at others. This occurred in one of the cases. At the first examination a diverticulum was clearly seen, but its exact point of entry into the duodenum was not ascertained. In order to do this a second examination was undertaken but, in spite of the exercising of great care, no diverticulum could be identified. At the third examination the diverticulum was found easily, and was seen to arise from the superior aspect of the third portion of the duodenum.

COMPLICATIONS

As would be natural to assume, a diverticulum may be the seat of varying degrees of inflammatory reaction. If the diverticulum has a wide mouth with adequate drainage, the relative sterility of the contents is a factor against the onset of inflammatory reaction. However, when drainage is inadequate, as when the neck is narrow or the ostium is concealed among the plica circulares of the duodenum, conditions are favorable for the setting in of inflammatory processes. As in the case of the diverticulum resected from the first part of the duodenum, the inflammation may be acute. Ulceration also may take place within the diverticulum. In one patient in this series a diverticulum was discovered in the first portion of the duodenum. Within this diverticulum a definite ulcer crater could be seen. This was the only positive finding in the gastrointestinal tract, and the patient was suffering with severe peptic ulcer-type symptoms. She was placed under strict ulcer regime, and immediate improvement took place. At her last visit she was entirely asymptomatic.

Ulceration within the diverticulum may progress to actual perforation. As in the appendix, an inflamed diverticulum whose neck is obstructed may perforate. This has been known to take place, and several reported cases may be found in the literature. Recovery of patients following surgical removal of acutely perforated duodenal diverticula has been reported. On the other hand, Boland[5] tells of a case in which a perforated diverticulum was overlooked at operation because the possibility of such an occurrence was not recognized. Ulceration within the diverticulum may also result in hemorrhage, which may be massive. There are a number of reports in the literature where patients have been cured of recurrent gastrointestinal hemorrhage by excision of the diverticulum. One such case was seen in this series and was successfully treated by medical means.

A diverticulum may be the seat of neoplastic change. There are at least six reports in the literature of primary neoplasms, both sarcoma and carcinoma, occurring within a diverticulum.

Duodenal diverticula often have been known to contain calculi, in fact the first diverticulum to be described (Chomel) was found to contain a large calculus. In one case in this series a calcification was noted within the diverticulum. These calculi are seen in perivaterian diverticula, and therefore usually are considered to have entered the diverticulum via the common duct. However, it is possible, in a diverticulum in which there is a sufficient degree of stasis, for calculi to be formed about bacteria or other debris. A calculus as large as 2 inches in diameter has been reported by Rankin.[32]

Another complication caused by diverticula of the duodenum is obstruction, which may be of the pancreatic, duodenal, or biliary system. A spread of inflammation may cause peridiverticulitis, which, in turn, may bring about the formation of adhesions which may cause trouble. The formation of cholecystoduodenal fistulas have been reported, and reports of other complications, such as duodenitis, cholangitis, and acute and chronic pancreatitis are also to be found in the literature.

SYMPTOMS

In almost every article on this subject it is stated that there is no characteristic symptom complex from which one may make a positive diagnosis of diverticulum of the duodenum. When roentgenologists first began to discover the presence of the lesion, it was felt that all should be attacked surgically. It was not until 1920 that Cole[11] allowed that "it *may* be true in some instances that duodenal diverticula are *not* the cause of clinical symptoms." Through the years the finding became more and more common and less and less significant in the eyes of the observers. At the present time most authors state that the majority of the pouches are not of much importance as they do not cause symptoms, and one is forced to agree with that observation. Unfortunately, however, because of this most diverticula are passed over almost as a normal finding. It is important to remember the fact that some diverticula, small as that percentage may be, are the seat of pathologic processes, and definitely do cause symptoms. There is the possibility of several complications with dire results that must be borne in mind, and to realize that a diverticulum is a latent source of such trouble one merely has to glance at the reports in the literature.

Morton[27] believes that there are three factors from which the symptoms may arise: (1) mechanical factors, (2) inflammatory reactions, (3) development within the diverticulum of a neoplasm. These factors may be further broken down. A diverticulum may give rise to symptoms when it is the seat of (a) stasis, (b) distention, (c) inflammation, which may range from mild to ulceration, (d) hemorrhage, (e) perforation, (f) neoplastic change. It was with stasis and inflammation in mind that duodenal drainage with culture was carried out in patients with and without duodenal diverticula. However, no etiologic factor was brought to light, all cultures resulting in the growth only of a diphtheroid.

Symptoms may be caused by pressure upon the common duct or by obstruction of the duodenum by pressure of a large dilated diverticulum, by pressure upon the pancreatic duct or another of the surrounding structures, by partial obstruction of the duodenum by pressure or by encroachment upon its lumen. A pseudodiverticulum will cause such encroachment, while a genuine diverticulum will not.

The symptoms of duodenal diverticula may follow a gastric, duodenal, pancreatic, biliary, intestinal, or colonic pattern. Beals was unable to make out any symptom complex, and he divided the symptoms of his thirty-eight cases into three classes: (a) ulcer-type symptoms, (b) simple nausea and vomiting and upper abdominal pain, (c) vague minor symptoms. To these, I believe should be added (d) gall bladder disease-type symptoms. It is of importance to note that, of the ninety patients, twenty-three were found to have peptic ulcer and twelve had gall bladder disease in addition to duodenal diverticula. Thirty-two had either ulcer or gall bladder disease or both. However, the symptomatology must be gone into in greater detail if any sort of picture is to emerge that may be called typical.

In this study an attempt has been made to elicit a group of signs and symptoms which, taken together, may enable one to make a presumptive diagnosis of duodenal diverticulum even before the carrying out of x-ray studies. This has been successful to a certain extent.

The symptoms complained of by the patients in this series have been pain, constipation, belching of gas, nausea, vomiting, and loss of weight in that order. However, if the thirty-two patients with peptic ulcer and/or gall bladder disease are disregarded, the symptoms, in the order of their occurrence, are constipation, belching of gas, nausea, pain, vomiting, and loss of weight.

A surprising fact is that constipation was the most common complaint, and was found to be present in as many as 46.5 per cent of the patients. In this the result of this study differs from that of other writers, and, in particular, the European authors who lay great stress upon the importance of the occurrence of diarrhea in patients with duodenal diverticula. They describe this diarrhea as consisting of about five to six stools per day, lasting for four or five days and then subsiding. This diarrhea apparently is caused by pancreatic disturbance. In this study diarrhea was not found to be a significant feature. In fact, it occurred so seldom that its importance as a feature in the clinical picture of duodenal diverticulosis or diverticulitis was disregarded.

The next most constant symptom was the belching of gas. This was complained of by 38.9 per cent of the patients, and, as a rule, resulted in relief of the discomfort to a greater or lesser extent. The belching of gas may be explained by the partial obstruction of the duodenum brought about by pressure of the diverticulum. The excessive amounts of gas are produced by fermentation of food particles retained within the diverticulum.

Thirty-three and seven-tenths per cent of the patients complained of nausea. The occurrence of nausea is easily understood when one recalls the physiologic fact that distention of the duodenum causes nausea. Thus it is

understandable that distention of the diverticulum or distention of the duodenum due to partial obstruction by pressure of the diverticulum would cause nausea.

Pain was found to be present in just 50 per cent of the total number of patients in the series studied. However, when the patients with peptic ulcer and/or gall bladder disease are disregarded, 33 per cent of the remainder complained of pain. In this group are included the patients with complaints varying from epigastric and upper abdominal distress to actual pain. The character of the pain depends upon the structures upon which pressure is exerted. This discomfort or pain is situated mostly in the right upper quadrant, but centered more toward the umbilicus than one would expect in the case of gall bladder disease. The patients frequently would complain of pain going through to the back between the shoulder blades, and also below the costovertebral angles. The pain caused by diverticula in the third portion of the duodenum is situated nearer the center, while that caused by pressure upon the pancreas is situated on the left. Other authors have mentioned pain as being present in as many as 85 per cent of their patients. It should be mentioned that in this series patients who complained of a sensation of bloating were not placed in this group. The significant feature of this pain is the fact that it usually can be relieved by causing the patient to assume certain postures, presumably positions that best would aid in the emptying of the sac. This pain usually comes on after meals, and, once relieved, does not recur until after the next meal.

Vomiting was complained of by 17.2 per cent of the patients, and is readily explained by distention of the diverticulum and obstruction of the duodenum by a large and distended sac.

Weight loss, although emphasized by several authors, was complained of by only a small percentage of the patients in this series.

One patient in this series, in whom the only positive finding was a diverticulum in the second portion of the duodenum which retained barium for six hours, gave a history of abdominal discomfort with repeated attacks of jaundice. The jaundice could not be demonstrated at any time during the hospitalization, and the discomfort subsided rapidly under medical management. The jaundice apparently was caused by pressure upon the common duct.

Symptoms caused by diverticula of the duodenum have been known to simulate exactly carcinoma of the head of the pancreas.

DIAGNOSIS

X-ray examination of the upper gastrointestinal tract still remains the only definite mode of diagnosis at the present time. However, a presumptive diagnosis of duodenal diverticulum may be made on the grounds of the symptoms. In a patient who is bothered with abdominal distress which may amount to pain, constipation, and belching of gas with or without nausea, and in whom there is a fairly constant area near and to the right of the umbilicus, pressure

upon which aggravates the discomfort, a diagnosis of duodenal diverticulum may be made with reasonable assurance. If the discomfort can be relieved by postural changes, the diagnosis can be made with even greater surety. It is necessary to remember, however, that in some instances it may not be possible to cause the diverticulum to empty in this manner, and in such patients no relief will be obtained by change of posture.

Duodenal drainage with examination of the specimen under the microscope and by culture adds nothing except in the case of hemorrhage from a diverticulum. In such a case, the repeated drawing of specimens during the passage of the tube through the duodenum, and the frequent checking of the position of the tube by examination under the fluoroscope will help in identifying the point of hemorrhage. Gastric analysis has not been found to be of any value. The only method of clinching the diagnosis is by careful x-ray examination. Several complicated maneuvers for filling the diverticulum with barium have been evolved, and are reported in the literature by the radiologists. However, it would appear that in most cases in which the diverticulum is causing the symptoms such elaborate measures would be found to be unnecessary.

In attempting to make the diagnosis of duodenal diverticulum, fluoroscopic examination should never be omitted. An important diagnostic point is palpation of the abdomen while the patient is being examined fluoroscopically after having ingested a barium meal. The point of tenderness under these conditions will be significant, and it is often possible to manipulate the filled diverticulum and thus to reproduce the distress or pain complained of by the patient, and also, by pressure, to empty the pouch and so relieve the discomfort until the sac fills again.

TREATMENT

The patients with duodenal diverticula, and in whom it is established that the diverticula are the cause of symptoms, may be divided into two groups: (1) those who can receive adequate relief by conservative means from medical management and (2) those who require surgical intervention.

Medical Management.—This consists of the correction of dietary faults and the institution of a bland diet. The use of antispasmodics, rest, regulation of bowel movements, and gentle massage are of value. A point that has been found to be of great value to patients in this series is postural drainage of the diverticulum. A simple method of ascertaining the best posture is for the patient to assume various positions while carrying out a gentle massage of the abdomen, particularly over the area of discomfort. The position which results in relief of the symptoms is the best for emptying the sac. The surest method of ascertaining this position is by fluoroscopic examination after the patient has swallowed a barium meal. Nearly all the patients in this series, except those operated upon, in whom it was felt that the seat of the trouble lay in the diverticulum, were relieved greatly of their symptoms by following this line of treatment, and have been almost entirely symptom free at their follow-up visits.

Surgical Management.—There has been a considerable swing of the pendulum with regard to opinion on this subject. At first it was felt that surgery was imperative in every case of duodenal diverticulum. There was then a swing to the other extreme so that all diverticula were looked upon as inconsequential and even normal findings. The pendulum now appears to be swinging back so that, at the present time, there is in the literature a considerable amount of discussion as to the need of operation for this condition. Admittedly the greater number of diverticula are symptomless and should be left alone. However, there is a small percentage in which the diverticula definitely are the source of trouble, and it is in these patients that surgery should be undertaken. This figure has been estimated by Pearse to be 5 per cent. This may appear to be a very high figure, but it should be borne in mind that it is a percentage that pertains, not to the general population, but only to those patients who have duodenal diverticula.

Before surgery is undertaken, careful evaluation of the patient's symptoms and exhaustive studies are of great importance, for otherwise the case is likely to be only a source of grief to the surgeon. These studies should include cholecystograms and gastrointestinal x-ray studies, a careful and painstaking search being made for peptic ulcer or any other lesion that may be the cause of the patient's symptoms.

According to Morton[27] there is justification for surgery on the following grounds:

1. Mechanical
   a. Symptoms from stasis within the diverticulum
   b. Symptoms from obstruction of the biliary tract, pancreas, or duodenum
2. Inflammatory
   a. Primary diverticulitis or hemorrhage, perforation, abscess, or peritonitis
   b. Secondary inflammation of the biliary tract, pancreas, duodenum, or retroperitoneal tissues.
3. Neoplastic change.

If there is inflammation within the diverticulum, and this goes on to cause hemorrhage, gangrene, perforation, or peritonitis, or if a neoplasm arises within the diverticulum, the question of surgery presents no problem. The great difficulty arises in deciding that the diverticulum is causing the symptoms from stasis or obstruction.

Retention of barium within the sac is an important factor in the diagnosis, and when this is associated with tenderness at that time it is still greater evidence that the diverticulum is at fault. It is generally agreed that retention here means the persistence within the diverticulum of barium for a period of six hours or more.

Surgical excision of a diverticulum of the duodenum is not as simple a procedure as one at first may be led to expect. There is a considerable amount of risk involved, and therein lies an additional reason as to why it is so im-

portant to establish the fact that the symptoms are being caused by the diverticulum before resorting to excision. Lahey[22] goes so far as to term a diverticulum a "mystifiable hazard."

When operation is undertaken, a careful search must be made for the presence of some other lesion which may account for the symptoms. Two patients in this series were operated upon because a diagnosis of duodenal diverticulum was made. In one of these patients a gall bladder filled with calculi was discovered and removed. This patient has been having a recurrence of symptoms. In the second patient a large diaphragmatic (esophageal hiatus) hernia was repaired, and the diverticulum was left intact. The patient has had complete relief of symptoms since operation.

When operation is performed, several different procedures may be carried out. Undoubtedly the procedure of choice is total excision of the lesion. However, when the sac lies in close proximity to the common and pancreatic ducts, or, as is sometimes the case, when the ducts open into the neck of the pouch, excision of the lesion with tight closure of the defect carries with it the dangers of damage to or obstruction of the ducts. In such a case it is most tempting to carry out a simple inversion of the sac. According to Barnes,[3] when diverticula invert themselves or are inverted surgically they sometimes continue to enlarge and fill up with a gelatinous type of material and eventually may produce acute or chronic intestinal obstruction. It is difficult to understand how or why such an occurrence should take place, and Barnes does not give the source of his information and does not report such an occurrence in any of his cases. It is conceivable that the inversion of a very large diverticulum by its size may produce intestinal obstruction, but the inversion of a small diverticulum should cause no trouble. Many authors have reported inversion without untoward effect. If nothing else, simple inversion precludes the possibility of duodenal leakage. According to Finney, intestinal obstruction may be brought about by the formation of fibrous tissue in the bowel through the influence of repeated infection in the duodenum extending into the intestinal wall. The bowel wall thus becomes infiltrated, thickened, and distorted, and ceases to function.

Operation performed for a diverticulum of the first part of the duodenum does not present many difficulties in exposure or approach. In the two patients in this series in whom such diverticula were removed, a subtotal gastrectomy was performed for peptic ulcer.

Diverticula in the second portion of the duodenum present greater problems. Some surgeons have dissected through the pancreas or have separated the pancreas from the duodenum. These methods, besides being of considerable difficulty, carry with them the very real dangers of pancreatic leakage and troublesome bleeding. Surgical approach, however, is not the only difficulty. Identifying the diverticulum and its position is also a real problem. Two methods have been advocated that may lead toward the solution of the problem. One, mentioned by Finney[14] and Walzel[36] and stressed by Mahorner,[26] is that of distending the duodenum with air, thereby causing the

diverticulum to distend and become more easily identifiable. The other method is that of MacLean,[24] who stresses the importance of opening the duodenum by means of a vertical incision in the descending portion and inserting an exploring finger which invariably will enter the diverticulum. The sac then is disposed of as desired, and the opening in the duodenum is closed transversely to obviate the possibility of causing a diminution in the size of the lumen of the duodenum.

The dissection carried out to isolate the diverticulum may injure the pancreaticoduodenal vessels, the pancreatic duct, or the common bile duct. Closure of the defect in the duodenum caused by the excision of the sac may injure or obstruct these structures. Pearse,[29] therefore, has suggested maneuvers directed toward the obviating of these dangers. He advocates approaching the duodenum from the lateral or convex aspect. The posterior peritoneum to the right of the duodenum is incised, and the duodenum is rotated toward the left until the diverticulum can be identified and drawn out toward the right. This is not difficult, as the diverticula usually arise from the posteromedial aspect of the duodenum.

The approach to diverticula in the third portion of the duodenum again presents certain difficulties. Morton mentions the relative inaccessibility of diverticula in this location, and advocates approaching them through the transverse mesocolon, the undersurface of the duodenum being exposed by dividing the retroperitoneal tissues. In order to obtain complete exposure it may be necessary to divide the ligament of Treitz. Mahorner, however, states that if the diverticulum is to the right of the mesenteric vessels, they can be exposed quite easily by dividing the superior leaf of the transverse mesocolon, and that it is not necessary to use the approach from below, which is a much more difficult and formidable undertaking. The approach to the diverticula to the left of the mesenteric vessels may be carried out very readily from below the transverse mesocolon. The diverticula are approached quite easily by incising the inferior leaf of the mesocolon to the left of the middle colic artery.

There are several methods of disposing of the diverticula depending upon their size, accessibility, and location. Simple inversion has been carried out by several surgeons with uniformly good results. A short circuiting operation has been advocated by others, but the results of such an operation have not been satisfactory, and a short circuiting should be carried out only in the case of multiple diverticula, where excision of all the diverticula cannot be carried out. The procedure of choice, of course, is that of total excision of the lesion.

In the case of diverticula other than the perivaterian, the only difficulty may be that of approach and exposure. However, in the excision of the perivaterian diverticula a very great danger is that of injury to the common bile duct or to the pancreatic duct or to both. The method advocated by Pearse is one that greatly lessens the dangers of injury to the ducts. The diverticulum, having been exposed from the right side of the duodenum, is trans-

illuminated and opened, following which it is excised, a cuff of tissue being left to prevent encroachment upon the lumen during closure. A catheter is passed into the common bile duct and out into the duodenum, and a probe is passed into the pancreatic duct from the duodenum. If preferred, probes may be passed into both ducts from the duodenal end. These are left in place while the first row of sutures is placed, thus ensuring against injury to these structures or their obstruction as closure is carried out.

In this series one diverticulum was excised from the second portion of the duodenum. This patient presented the typical symptoms of abdominal distress with a burning sensation in the epigastric region, gaseous discomfort with belching, nausea, and constipation. The diverticulum was excised using the method advocated by Pearse. This patient has been entirely symptom free on her follow-up visits.

DISCUSSION

Most authors state that a diverticulum of the duodenum is of no significance, and many go so far as to state that it is not an abnormal finding. They feel that when a diverticulum is discovered, it merely amounts to proof that the radiologist has examined the duodenum with care. On the other hand, others have written of the symptoms proved to have been caused by the diverticulum, and cases citing examples of formidable complications and dire results are not lacking in the literature. What then is the attitude that one should take? What is the actual significance that one should attach to the finding of a diverticulum of the duodenum? The logical and most sensible view that one could take would be to follow neither one extreme course nor the other, and to steer a course in between the two, striking the happy medium and judging each case upon its merits. Admittedly by far the greater number of diverticula are innocent and cause no symptoms. The fact remains, however, that a small percentage of diverticula *do* cause trouble which may amount to anything from mild annoying and distressing symptoms to dangerous and even fatal complications.

A patient in whom a duodenal diverticulum has been discovered should be submitted to a careful and thorough examination in order that any other possible cause of the symptoms may be brought to light. At the same time it should be borne in mind that even in the presence of other additional disease the diverticulum may be the cause of some or all of the symptoms. In one case in this series a diverticulum of the first part of the duodenum was removed duing the course of a subtotal gastrectomy for peptic ulcer. On pathologic examination this diverticulum was found to be the seat of acute inflammation. One would not be far wrong in assuming, therefore, that at least some of the symptoms complained of by the patient were caused by this diverticulitis. It would be impossible to make any statement as to where the symptoms of diverticulitis ended and those of the ulcer started, for both lesions were excised with complete relief to the patient.

It already has been stated that when a patient with a diverticulum has symptoms, extensive and intensive examinations should be carried out for

another possible source of the trouble. One should also remember that when a patient complains of symptoms for which no cause can be found, a search should be made for a diverticulum of the duodenum.

Weintraub and Tuggle[39] state that if a diverticulum is diseased and is producing symptoms, it should show, on x-ray examination, one or more of the following signs: (a) localized tenderness, (b) changes in the mucosal pattern of the diverticulum such as a persistent fleck, (c) mucosal changes in the adjacent duodenum, (d) irritability of the duodenum, (e) stasis. Actually it is only when the diverticulum is demonstrated on x-ray examination that the diagnosis can be made with any definite degree of certainty—and then there still remains the problem of correlating the presence of the diverticulum with the symptoms complained of by the patient. Cholecystograms and gastrointestinal x-ray studies should, therefore, be carried out in all cases. Great stress is laid on stasis in the diverticulum, but this point does not appear to be as significant as one would be led to believe, for in this series several patients had symptoms caused by the diverticula, while on x-ray examination no significant degree of stasis could be demonstrated within the diverticulum.

The pendulum of opinion on this subject has swung from one extreme to the other, and now is swinging back. Perhaps it will swing to the middle and there be stopped so that the diverticulum of the duodenum will be afforded the significance due it, for obviously neither one extreme view nor the other is right, and a persistence in either school of thought can but end in grief.

REFERENCES

1. Ackerman, W.: Diverticula and Variations of the Duodenum, Ann. Surg. **117**: 403, 1943.
2. Baldwin, W. M.: Duodenal Diverticulum in Man, Anat. Rec. **5**: 121, 1911.
3. Barnes, F. L.: Diverticulosis of the Duodenum, Am. J. Surg. **20**: 328, 1933.
4. Beals, J. A.: Duodenal Diverticula, South. M. J. **30**: 218, 1937.
5. Boland, F. K., Jr.: Acute Perforated Duodenal Diverticulum, SURGERY **6**: 65, 1939.
6. Boyd, W.: Surgical Pathology, ed. 6, Philadelphia, 1947, W. B. Saunders Company, p. 255.
7. Boyd, W.: Textbook of Pathology, ed. 4, Philadelphia, 1943, Lea & Febiger, p. 491.
8. Browne, D. C., and McHardy, G.: Duodenal Diverticulitis, Acute and Chronic, New Orleans M. & S. J. **95**: 553, 1943.
9. Case, J. T.: Roentgen Observations on the Duodenum With Special Reference to Lesions Beyond First Portion, Am. J. Roentgenol. **3**: 314, 1916.
   Diverticula of Small Intestine Other Than Meckel's Diverticulum, J. A. M. A. **75**: 1463, 1920.
10. Chomel, J. B. L.: Historie de L'Academie Royale, Paris, 1710.
11. Cole, L. G., and Roberts, D.: Diverticula of the Duodenum, Surg., Gynec. & Obst. **31**: 376, 1920.
12. Edwards, H. C.: Diverticula of the Duodenum and Jejunum, Lancet **1**: 169, 1934.
    Diverticula of the Duodenum, Surg., Gynec. & Obst. **60**: 946, 1935.
    Diverticulosis of the Small Intestine, Ann. Surg. **103**: 230, 1936.
13. Ehrenpreis, B.: The Roentgen Diagnosis of Meckel's Diverticulum, Am. J. Roentgenol. **42**: 280, 1939.
14. Finney, J. M. T., Jr.: Duodenal Diverticuli; Their Significance and Treatment, South. Surgeon **11**: 543, 1942.
15. Fletcher, H. N., and Castleden, L. I. M.: Three Cases of Duodenal Diverticulum Removed by Operation, Brit J. Surg. **23**: 776, 1935-36.
16. Forssell, G., and Key, E.: Ein Divertikel der Pars descendens duodeni mittels Roentgenuntersuchung diagnostiziert und operativ entfernt, Fortsch. a. d. Geb. d. Roentgenstrahlen **24**: 48, 1916.
17. Friedlander, G.: Diverticula of Duodenum, Brit. J. Radiol. **10**: 26, 1937.

18. Grant, J. C. B.: On Frequency and Age Incidence of Duodenal Diverticula, Canad. M. A. J. **33**: 258, 1935.
19. Hansemann, D.: Virchows Arch. f. path. Anat. **144**: 400, 1896.
20. Keith, A.: A Demonstration on Diverticula of the Alimentary Tract of Congenital or of Obscure Origin, Brit. M. J. **1**: 376, 1910.
21. Kyle, H. M.: The Biology of Fishes, New York, 1926, The Macmillan Company, p. 125.
22. Lahey, F. H.: Surgery of the Duodenum, New England J. Med. **222**: 444, 1940.
23. Linsmayer, H.: Ueber Duodenaldivertikel, Verhandl. d. deutsch. path. Gesellsch. **17**: 445, 1914.
24. MacLean, N. J.: Diverticulum of the Duodenum, Surg., Gynec. & Obst. **37**: 6, 1923.
25. Mahorner, H.: Diverticula of the Duodenum, Ann. Surg. **133**: 697, 1951.
26. Mahorner, H., and Kisner, W.: Diverticula of the Duodenum and Jejunum, Surg., Gynec. & Obst. **85**: 607, 1947.
27. Morton, J. J.: The Surgical Treatment of Primary Duodenal Diverticula, SURGERY **8**: 265, 1940.
28. Odgers, P. N. B.: Duodenal Diverticulosis, Brit. M. J. **17**: 592, 1930.
29. Pearse, H. E.: The Surgical Management of Duodenal Diverticula, SURGERY **15**: 705, 1944.
30. Pendergrass, R. C.: Roentgen Diagnosis of Duodenal Diverticula, Radiology **17**: 1216, 1931.
31. Rankin, F. W., and Martin, W. J., Jr.: Diverticula of Small Bowel, Ann. Surg. **100**: 1123, 1934.
32. Rankin, L. M.: Diverticula of the Duodenum, Am. J. Roentgenol. **47**: 585, 1942.
33. Rosenthal, T.: Können Duodenaldivertikel eine klinische Bedeutung erlangen? Med. Klin. **4**: 1421, 1908.
34. Thorek, M.: Duodenal Diverticulum With Ulcer, Illinois M. J. **55**: 64, 1929.
35. Turner, F. C.: Tr. Path. Soc. Lond. **35**: 200, 1884.
36. Walzel, P.: Ein Behelf zur Darstellung schwierig oder nicht auffindbarer Duodenaldivertikel wahrend der Operation, Zentralbl. f. Chir. **62**: 1206, 1935.
37. Warren, H. A., and Emery, E. S., Jr.: Duodenal Diverticula With Special Reference to Their Symptomatology, Gastroenterology **1**: 1085, 1943.
38. Weig, C. G.: Benign Ulceration Within a Duodenal Diverticulum, Radiology **48**: 143, 1947.
39. Weintraub, S., and Tuggle, A.: Duodenal Diverticula, Radiology **36**: 297, 1941.

Surgical Technique

A MORE RAPID OPERATIVE TECHNIQUE FOR ESOPHAGECTOMY

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THE most satisfactory surgical procedure at present for lesions of the middle one-third of the esophagus seems to be mobilization of the stomach, resection of the lesion, and esophagogastrostomy. This paper describes operative techniques that reduce the time necessary for the operation and briefly reports three cases exemplifying this advantage without sacrifice of exposure and extent of resection.

Overlapping of the operative stages to shorten duration of the combined right thoracic and left abdominal approach for lesions of the upper and middle portions of the esophagus has been proposed by Harrison and Picket.[2] The use of two teams, operating simultaneously, one in the abdomen and one in the chest, was suggested by one of us (F. R.).

A complete description of the accepted technique of esophagectomy need not be repeated here. Discussion will be confined, therefore, to the modifications of the technique employed by us.

MODIFICATIONS OF SURGICAL TECHNIQUE

The patient is placed slightly on the left side. The right shoulder is elevated and drawn to the left sufficiently to result in approximately a twenty-degree angle of the thorax with the horizontal. This results in a mild axial rotation of the chest on the abdomen and leaves the abdomen nearly level. If a cervical incision is contemplated, the right arm is draped in sterile stockinet. This allows sufficient mobility of the arm and shoulder to permit cervical dissection (Fig. 1).

The chest operator places himself on the patient's right and his assistant is opposite. The abdominal operating team is reversed. Because we feel that virtually all lesions should be resected, even though palliative, we do not wait for operability to be determined. The chest is opened through a posterolateral thoracotomy incision resecting the fifth rib. The esophagus with its lesion is

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then mobilized. Simultaneously, a long left paramedian abdominal incision is made and the stomach is mobilized. The hiatal dissection is expedited by the two operators working toward each other. The stomach is then passed into the chest after a Ramstedt pyloromyotomy has been performed. As soon as the abdominal procedure is completed, the abdomen is closed.

Following resection of the lesion the esophagogastric anastomosis is performed in the manner described by Sweet.[6, 7] The chest is closed in routine fashion. Pleural drainage is employed.

Fig. 1.—Diagrammatic sketch illustrating the patient's position and incisions for simultaneous two-team esophagectomy.

CASE REPORTS

The first two patients in whom this procedure was employed were white men aged 57 and 67 years. Both had epidermoid carcinoma of the mid-portion of the esophagus. In each instance esophagogastrostomy was performed at the level of the third thoracic vertebra. The operative periods were three and three-quarters and three and one-half hours, respectively. The third patient was a 28-year-old white man with an extensive esophageal stricture caused by lye, that required cervical esophagogastrostomy; elapsed time was four hours.

Transient operative shock was observed in one patient; it was due to excessive loss of blood from inadvertent fracture of the spleen. All three patients are doing satisfactorily thus far during the thirteen, ten, and nine months, respectively, since operation.

SUMMARY

A modification of the combined right thoracic and left abdominal approach for treatment of lesions of the esophagus is presented. Its trial in three cases demonstrates that it sacrifices none of the advantages of this approach,[1-5] and, without increase in morbidity, shortens the operative time.

REFERENCES

1. Gaspar, Max, and Snyder, E. N., Jr.: Surgery of the Esophagus Through the Right Chest, Am. J. Surg. **84**: 306-312, 1952.
2. Harrison, A. W., and Picket, W. H.: One-Stage Multiple Approach Operation for Cancer of the Upper and Mid-Thoracic Esophagus, SURGERY **28**: 771-778, 1950.
3. Kent, E. M., and Harbison, S. P.: The Combined Abdominal and Right Thoracic Approach to Lesions of the Middle and Upper Thirds of the Esophagus, J. Thoracic Surg. **19**: 559-571, 1950.
4. Lewis, Ivor: The Surgical Treatment of Carcinoma of the Esophagus With Special Reference to a New Operation for Growths of the Middle Third, Brit. J. Surg. **34**: 18-31, 1946.
5. Macmanus, J. E.: Combined Left Abdominal and Right Thoracic Approach to Resection of Esophageal Neoplasms, SURGERY **24**: 9-16, 1948.
6. Sweet, R. H.: Carcinoma of the Superior Mediastinal Segment of the Esophagus, SURGERY **24**: 929-938, 1948.
7. Sweet, R. H.: Thoracic Surgery, Philadelphia, 1950, W. B. Saunders Company.

Book Reviews

La Chirurgie du Rein en fer a Cheval. By P. Macquet and L. Wemeau. Pp. 102, with 39 illustrations. Paper covers, uncut pages. Paris, 1952, Masson & Cie.

French medical monographs have two outstanding weaknesses: they are written in French which, as Ruggles of Red Gap long ago observed, is not only badly misspelled but also atrociously mispronounced according to English standards; the French publishers also leave it to the avid reader to do a lot of cutting to find out what is on the other side of the page.

This book is a review of the subject of horseshoe kidney based upon a survey of the literature (eighty references) and upon experience with eleven patients. Included are reviews of anatomy and embryology. The authors believe that the mere presence of horseshoe kidney may cause renal pain in the absence of complicating disease, although but one of their eleven patients could be placed in this category. The reviewer has never seen a painful horseshoe kidney in the absence of hydronephrosis or stone, nor can he accept the undocumented statement of the authors that the average patient with a horseshoe kidney will die at 40 or 45 years unless operated upon fairly early in life.

Recognition of the anomaly by means of urography and retroperitoneal pneumoradiography is discussed in detail. Of their eleven patients, three had hydronephrosis, four had stone, two tuberculosis, one posttraumatic cicatrization, and one had hypertension. Of the two without complicating disease, one had symphysiotomy for pain, and one had no symptoms and was not treated.

The technique of renal symphysiotomy through a lumbar extraperitoneal approach is discussed. The book is interesting to the urologist but contains nothing new.

Frontal Lobotomy and Affective Behavior. By John F. Fulton, M.D., Professor of History of Medicine, Yale University. Pp. 159, with 20 illustrations. New York, 1951, W. W. Norton & Company, Inc.

The material in this book was given by Dr. Fulton as a series of Salmon Memorial Lectures, and concerns human and primate behavior as effected by specific lesions of the forebrain.

Chapter I is a brief, but interesting, review of the discovery of the localization of cortical function. The contributions of Jackson, Ferrier, and Sherrington are briefly recounted. Both Ferrier and Bianchi ablated the frontal lobes in monkeys and objectively described their observations. This was before the time of the conditioned reflex technique of Pavlov and the learning techniques which were later utilized by Thorndike, Franz, Yerkes, and others. With the use of these new techniques in which the animals were trained or taught certain skills before ablation operations were performed, much was learned concerning the function of the cerebral cortex, especially the visual cortex. Jacobson was the first to apply these modern training methods of psychobiology to the function of the orbitofrontal cortex.

Chapter II continues with certain historical and scientific aspects of the topic. Although the Russian physiologist Bechterew and Pavlov previously had realized that there was a central representation of autonomic function, Langley considered the autonomic nervous system to be a purely peripheral motor system without functional relation with other parts

of the brain and spinal cord. The recognition of autonomic function in the hypothalamus by Karplus and Kreidl, and the investigation of this function by them and others is described at some length.

The author concludes that bilateral frontal ablation removes an important ascending sensory system, mostly visceral in origin, from consciousness, and that this reduction in the nociceptive impulses reaching the cortex is the reason for relief of pain by frontal lobotomy. The relations between the neopallium and the visceral brain are discussed in detail.

Chapter III shows that recent experiments, consisting of transection of the fornix or of bilateral destruction of the hippocampus, indicate that the hippocampus is not essential for olfactory discrimination. This is confirmed in man by a lack of olfactory sensations when the hippocampus is stimulated. The effect of interruption of the hippocampus seems to be that it renders the animal more placid. Ablation of the posterior orbital gyrus results in hyperactivity, and this hyperactivity is apparently mediated through the caudate nucleus. In addition, ablation of this area affects autonomic or hypothalamic function. Excision of the entire area of the posterior orbital, anterior insular, temporal polar, and amygdaloid cortex results in the animal's being hyperactive, consuming excessive food, and developing a subnormal temperature due to vasomotor release. The animals in which this entire area was excised performed previously learned problems well, but they had abnormal behavior. After immediate reflex withdrawal from a noxious stimulus, they seemed to be quite unconcerned and returned immediately to the noxious situation. Also, they tended to put into their mouths everything movable within their visual horizon. Lesions of the insula caused no behavioral or intellectual deficit, but with bilateral insular ablation there was a temporary disturbance of taste. Bilateral destruction of the amygdala caused rage reactions in some animals, especially in cats, but most animals required a greater stimulus to be roused to activity, yet when activated they became quite vigorous. Destruction of the temporal lobe tip produced no hyperactivity, but otherwise these animals were to a lesser degree similar to the animals in which there was destruction of the posterior orbital, anterior insular, and amygdaloid cortex. Ablation of the anterior cingulate gyrus in the monkey caused the animal temporarily to become more tame without loss of intellect, as demonstrated by the delayed reaction test or problem boxes. These animals were not easily frustrated.

Chapter IV discusses lobotomy in man, especially in relation to recent developments with lesser operative techniques than the Freeman and Watts or Lyerly technique. The adaptation or selection of an operative procedure according to cerebral physiology, so that the procedure chosen will give maximum benefit for the condition present, is discussed.

It is concluded that for the depressed patient and the schizophrenic with subnormal motor activity, the proper operation should be a resection of the posterior orbital gyrus or an interruption of the projection fibers of this area. For the agitated, aggressive, and overly active psychotic patient, either a cingulectomy or a topectomy involving Brodmann's areas nine and ten should be the procedure of choice. However, with removal of areas nine and ten or their projections, there is always some degree of intellectual impairment. It is also concluded that visceral afferent fibers primarily concerned with the relief of pain pass through the medial ventral quadrant, and that by their selective division, pain can be relieved without accompanying intellectual deficit.

Pheochromocytoma and the General Practitioner. By Joseph L. DeCourcy and Cornelius B. DeCourcy. Cincinnati, DeCourcy Clinic. $4.00.

This book is a well-documented review of the literature on pheochromocytoma and a plea for suspicion of pheochromocytoma in all hypertensive states and in many others. While the book is said to be for the general practitioner, it appears to be too extensive and complex for this purpose. It constitutes, however, a well-directed plea for an attempt to diagnosis of this lesion which is so often missed.

Although organization of the book sometimes makes reading difficult (for example, an historical résumé which starts at the present and works backward), this volume would repay one's reading time with a wealth of information.

Hirndurchblutungsstörungen. By Dr. A. Brobeil. Pp. 264, with 84 illustrations. Stuttgart, 1950, Georg Thieme Verlag, Agent for U.S.A.: Grunc & Stratton, Inc., New York. DM 45.

This book is presumably written to present the information that has been gained by means of angiography about the cerebral blood vessels in cerebral disease. Since percutaneous angiography has become a very common procedure, there has been much opportunity to observe the blood vessels visualized by opaque media.

The book does, however, discuss almost every phase of intracranial circulation in a verbose manner. Beginning with a discussion of pathologic physiology of brain circulation, it discusses decreased blood flow in hemorrhage and heart disease and the reflexes that control the cerebral circulation. Complete sympathetic control of the intracranial vessels by the sympathetic nerves is accepted as being definitely established. The pharmacologic action of drugs, and its influence on the intracranial circulation, is discussed in a general manner without reference to angiography.

Dr. Brobeil discusses occlusion of the different intracranial vessels, beginning with the internal carotid artery. Etiology of occlusion receives attention, but much of the discussion concerns the differential diagnosis of the occlusion of each artery. It is indicated that filling of the anterior cerebral artery on the side opposite the injected carotid is due to a pressure gradient, the pressure being higher on the side injected under such conditions as compression of the internal carotid on the opposite side by a tumor, or when the pulse is slow and injection is made during diastole. Here the writer is assuming, and apparently without proof, that the injection increases the intracarotid pressure. Many pages are devoted to argument against the views of Kreig, because this author apparently said that such filling of the opposite side where the circulation is constricted or diminished is due to "blood attraction." Fifty-three pages are devoted to cerebral vascular crisis, which means both vasodilation and vasoconstriction. Included in these pages are long descriptions of migraine, Menière's syndrome, epilepsy, and some other conditions. In this section some normal angiograms are shown in connection with case reports.

Cerebral thromboangiitis obliterans, according to this author, is the cause of many encephalopathies that have in the past been considered to be degenerations of unknown etiology. Some of them were seen to have enlarged ventricles on air study, but the diagnosis was made mostly on the angiogram from the following changes: (1) increased tortuosity of the siphon, (2) defects in the arterial walls, (3) elongation of vessels, (4) narrowing of arteries, (5) absence of peripheral parts of the vessels, (6) absence of filling of the anterior cerebral artery, (7) absence of filling of the middle cerebral artery, or at least nonfilling of all its branches.

Sixteen cases of thromboangiitis obliterans are reported. In some the accompanying angiograms are quite convincing, in others they are not. Only one came to post mortem, and the disease was diagnosed thromboangiitis obliterans and polycythemia, but no microscopic pictures are shown.

The final forty-six pages are on cerebral arteriosclerosis. The author distinguishes three stages of severity of arteriosclerosis by angiography.

The first stage occurs when the diameter of the siphon is widened and has increased tortuosity with slight roughening of the lumen. Similar changes occur in the more peripheral arteries and there is a decrease in the filling of small peripheral vessels.

The second stage shows these same changes, but increased or more severe.

The third stage has gross defects in the lumen of the siphon. There is a very definite decrease in the contrast filled vessels, and some arteries such as the pericallosal and middle cerebral may end abruptly. There is absence of the peripheral vessels. The other changes of the two earlier stages are increased. The middle meningeal artery is more than normally filled.

Neurosurgery—An Historical Sketch. By Gilbert Horrax, M.D. Pp. 135, with 41 illustrations. Springfield, Ill., 1952, Charles C Thomas, Publisher. $3.75.

The History and Development of Neurological Surgery. By Ernest Sachs, M.D. Pp. 158, with 50 illustrations. New York, 1952, Paul B. Hoeber, Inc. $5.00.

These delightful monographs written by surgeons who have been eyewitnesses and participants in the great developments which have occurred in neurosurgery should be of great interest to all surgeons. Improved techniques whether in diagnosis or therapy—these are the items which have contributed to the advance of neurosurgery. This conclusion is quite inescapable as one recounts in almost every development the importance of improved techniques. Both monographs trace briefly the items which have contributed to the evolution of present-day practices in neurosurgery. There is much useful information in each monograph compressed by terse and well-ordered statement into a few pages.

This reviewer believes that these monographs can be of great service to anyone desirous of learning the processes of growth in a province of surgery. The manner of growth in each is probably quite the same. It might reasonably have been anticipated that the authors would lend a bit more emphasis to use of the experimental method in the development of neurosurgery. Neurosurgeons, more than other surgical specialists, have, especially in recent years, employed the experimental approach to great advantage in giving acceleration to the growth of knowledge in the broad aspects of neurosurgery.

The great neurosurgeons of the period covered by the authors were probably, with few if any exceptions, trained initially in general surgery. Today, many neurosurgeons affect to be able to teach their young protégés all they need to know of surgery. This reviewer believes that this practice does not augur well for the development of men like Cushing, Dandy, Adson, Peet, Penfield, Naffziger, Horrax, or Sachs.

These two interesting monographs by two well-known American neurological surgeons appeared in 1952. Though their manner of dealing with the subject matter is quite different, it is remarkable how similar the over-all treatment of this same theme by two keen contemporary proponents of neurosurgery is. The chapter headings are very much alike, and the choice of subjects for illustrations is very much the same, though the pictures are different. Horrax dedicated his monograph to Victor Horsley and to Harvey Cushing, whom he rightfully recognizes as the founders of neurosurgery. Sachs dates the beginning of modern neurological surgery from Dandy's publication on ventriculography in 1918.

A more complete and systematic account of the beginnings of neurosurgery and the modern period is to be found in the Sachs monograph which includes 540 references, whereas Horrax lists 181. A very complete, combined author and subject-matter index also enhances considerably the usefulness of the Sachs monograph.

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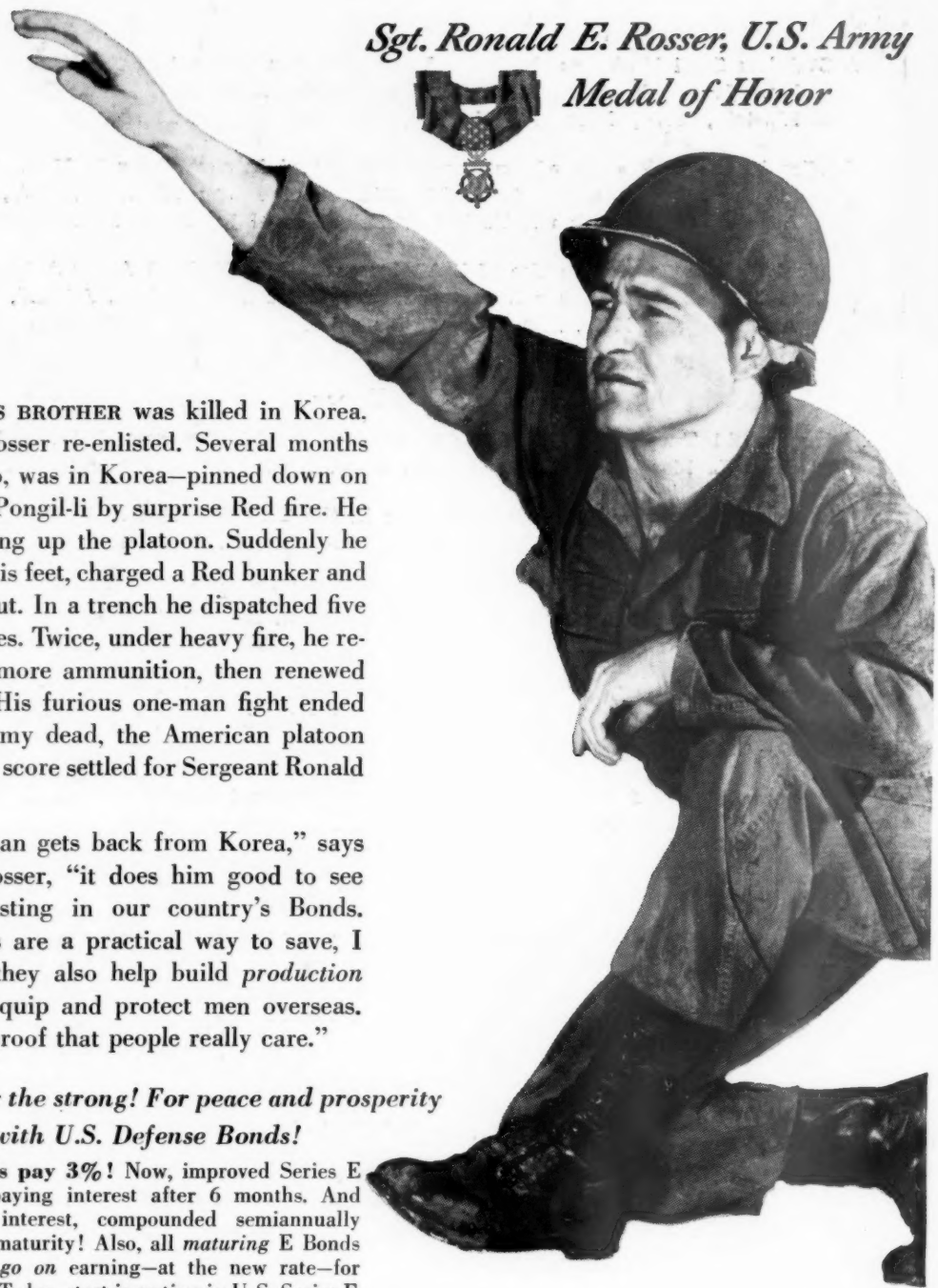

Sgt. Ronald E. Rosser, U.S. Army
Medal of Honor

WHEN HIS BROTHER was killed in Korea. Sergeant Rosser re-enlisted. Several months later he, too, was in Korea—pinned down on a hill near Pongil-li by surprise Red fire. He saw it cutting up the platoon. Suddenly he jumped to his feet, charged a Red bunker and cleaned it out. In a trench he dispatched five more enemies. Twice, under heavy fire, he returned for more ammunition, then renewed his attack. His furious one-man fight ended with 13 enemy dead, the American platoon saved, and a score settled for Sergeant Ronald Rosser.

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